Class PC261
Book T3
Copyright No.

COPYRIGHT DEPOSIT.

CANCER

ITS STUDY AND PREVENTION

BY

HOWARD CANNING TAYLOR, M.D.

GYNECOLOGIST TO THE ROOSEVELT HOSPITAL, NEW YORK; PROFESSOR OF CLINICAL GYNECOLOGY, COLUMBIA UNIVERSITY; MEMBER OF THE AMERICAN GYNECOLOGICAL SOCIETY, AMERICAN COLLEGE OF SURGEONS, AMERICAN SOCIETY FOR THE CONTROL OF CANCER, AMERICAN MEDICAL ASSOCIATION, NEW YORK OBSTETRICAL SOCIETY, ETC.

LEA & FEBIGER
PHILADELPHIA AND NEW YORK
1915

RC261
T3

Entered according to the Act of Congress, in the year 1915, by
LEA & FEBIGER,
in the Office of the Librarian of Congress. All rights reserved.

#250
AUG -5 1915

©CI.A406997

PREFACE.

No larger problem in public health confronts the medical profession and the laity of the civilized world today than that of cancer. The death of over 75,000 people yearly in the United States, and approximately a proportionate number in all countries where mortality statistics are obtainable, is proof of this statement.

There are two ways by which this problem can be approached: one is by the acquisition of more information regarding the disease, and the other by a better use of the facts now in our possession. To obtain more knowledge of the subject is the task of both the investigator in the laboratory and the clinician with his patients. To make more practical use of the facts relating to cancer which we now possess, is the duty of the clinician and of the patient. Throughout the entire world may be found institutions equipped to search for facts about cancer; and although even its cause remains undiscovered, additions to our store of information are being made almost daily by means of their researches. There is only praise for the work they are doing.

The opportunity and the obligation of the clinician to contribute to our knowledge of the subject are not grasped as clearly as they should be. Neither in this country nor in any other do proper statistics exist regarding cancer and the results of its treatment. It is the plain

duty of all practitioners to preserve more accurate records of patients afflicted with malignant disease. While thus employed in collecting additional data, it is equally the duty of the clinician to make the best use of those facts already available. Much valuable information is now obtainable which physicians should not only know but promulgate among the laity with the hope of materially lowering the death rate. Some cancers could be prevented, others could readily be cured.

The object of this book is to put together these facts and place them within easy reach of the profession and of others interested in this gigantic problem.

Throughout the following pages will be found, many times repeated, the statement that patients with cancer come too late for successful treatment. This is often the result of neglect of the first symptoms of the disease. The attempt has been made to indicate the causes of cancer so that it may be avoided if possible, to give the earliest symptoms by which the condition can be recognized, and to show that by early surgical interference, favorable results can often be obtained with small risk.

H. C. T.

New York, 1915.

CONTENTS.

CHAPTER I.

General Considerations.

Cause of Cancer 26
Predisposition to Cancer 37
Geographical Distribution 44

CHAPTER II.

Precancerous Lesions 50

CHAPTER III.

Contagiousness of Cancer.

Metastases 74
Extension by Contact or Implantation 79
Cachexia 84

CHAPTER IV.

Spontaneous Cure of Cancer.

Multiple Primary Cancers 99

CHAPTER V.

Carcinoma and Sarcoma of the Breast.

Carcinoma of the Breast 103
Sarcoma of the Breast 125

CHAPTER VI.

Carcinoma of the Uterus.

Carcinoma Uteri and Pregnancy 163

CHAPTER VII.

Carcinoma of the Oral or Buccal Cavity.

Carcinoma of the Tongue 176
Carcinoma of the Cheek 183
Carcinoma of the Palate 185
Carcinoma of the Gums 186
Carcinoma of the Lips 187
Carcinoma of the Face 194
Sarcoma of the Jaws 197

CHAPTER VIII.

Carcinoma of the Esophagus 204

CHAPTER IX.

Cancer of the Stomach 212

CHAPTER X.

Carcinoma of the Intestines—Sarcoma of the Intestines —Carcinoma of the Appendix—Cancer of the Rectum.

Carcinoma of the Intestines 244
Carcinoma of the Duodenum 247
Carcinoma of the Jejunum and Ileum 250
Carcinoma of the Large Intestine 251
Sarcoma of the Intestines 264
Carcinoma of the Appendix 268
Cancer of the Rectum 272

CHAPTER XI.

Carcinoma of the Gall-bladder and Ducts—Carcinoma of the Liver—Carcinoma of the Pancreas.

Carcinoma of the Gall-bladder and Ducts 284
Carcinoma of the Ampulla of Vater 291
Carcinoma of the Liver 292
Carcinoma of the Pancreas 297

CHAPTER XII.

Cancer of the Kidney, Bladder, Prostate, Penis, and Testis.

Cancer of the Kidney 301
Carcinoma of the Kidney 309
Sarcoma of the Kidney 309
Malignant Adenoma of the Kidney 310
Carcinoma of the Urinary Bladder 310
Carcinoma of the Prostate 315
Carcinoma of the Penis 318
Cancer of the Testis 320

CANCER.

CHAPTER I.

GENERAL CONSIDERATIONS.

Definition.—The word cancer is not strictly a scientific term, though it is in common usage both by the medical profession and the laity. Practically, it is synonymous with malignant tumor, malignant disease, and malignant growth.

The word tumor is used surgically, somewhat loosely, to mean any circumscribed swelling, even though it is not a new growth. For example, the swelling and induration of an abscess may be spoken of as a tumor. It would be better if the term were limited more strictly and used only to denote new growths.

If, however, the term tumor is qualified by the word malignant, it practically always means a new growth. A malignant tumor means a cancer.

The two common varieties of cancer are carcinomata and sarcomata. These terms are strictly scientific, and always indicate the same types of tumors. It is a mistake, however, to assume that all carcinomata or all sarcomata are the same, for they show the widest variations in their characteristics. The growth may be rapid or slow, metastases may form early or late, and the cachexia from the tumor may develop shortly after its onset or only after it has existed for some years.

For example, an epithelioma of the face may be of such mild degree of malignancy, that it may exist for years

and can often be cured by the simplest therapeutic measures, while an epithelioma of the tongue is of more rapid growth and more quickly passes the curative stage, and there is a strong tendency for it to return even after an extensive operation. The difference in the rate of growth in these two conditions is probably due to the difference in the location in which the growths are situated. On the face, the growth remains relatively quiet, and is not subjected to the frequent movements of a similar condition on the tongue. If a malignant tumor is constantly irritated or moved about, its rate of growth will be increased.

A scirrhus carcinoma in the breast is of a low grade of malignancy; it is of relatively slow growth, and may last for years. A medullary carcinoma in the same location is of a high grade of malignancy and rapidly forms metastases and becomes inoperable. The difference in the rate of growth in these two tumors is due to the difference in the variety of the tumor, though they are both carcinomata. The scirrhus carcinoma is of small size, and the growth and the breast in which it is situated together may be smaller than the opposite normal breast. The medullary carcinoma forms a large tumor.

These wide variations occur both in the carcinomata and in the sarcomata. It is possible, when the origin and cause of cancer are known, it will be found that there are a larger number of different varieties of cancer than is believed today.

It is not easy to give a definition of a malignant growth or cancer; it is easier to describe its characteristics.

Characteristics.—The characteristics of a cancer or of a malignant tumor are given by Delafield and Prudden as follows:

"1. Invasion of adjacent tissues by eccentric or peripheral growth.

2. The tendency to local recurrence after removal.

3. The formation of metastases.

4. An interference with the nutrition and general well-being of the body, which may give rise to a condition known as cachexia."

A benign tumor does not invade the adjacent tissues, but displaces or pushes them before it, and when removed, it does not tend to return either locally or at a distance.

A benign tumor may interfere with the general well-being and nutrition of the body by interfering with the action of important organs. For example, a benign tumor of the intestine may obstruct its lumen and indirectly interfere with the general nutrition of the body. A benign tumor, however, does not interfere with the general body nutrition by the production of toxins, as is believed to be the case with malignant growths.

Incidence and Increase in Frequency.—It is generally, though not universally, believed that cancer is increasing.

The following table gives the number and relative frequency of cancer deaths in England and Wales for different years since 1840:

Year.	Deaths from all causes.	Deaths from cancer.	Cancer deaths per 1,000,000 population.	Proportion of cancer deaths to living population.	Number of deaths from cancer to each 100 deaths.
1840 . .	359,687	2,786	177	1 to 5646	1 to 129
1860 . .	422,721	6,827	343	1 to 2915	1 to 62
1880 . .	528,624	13,210	502	1 to 1946	1 to 40
1900 . .	587,830	26,721	828	1 to 1207	1 to 22
1905 . .	520,031	30,221	885	1 to 1131	1 to 17
1912 . .	486,939	37,325	1019	1 to 980	1 to 13

There are several facts shown by this table. The fourth column shows that in 1840 there were recorded 177 deaths, and in 1912 there were recorded 1019 deaths from cancer in England and Wales for each 1,000,000 of population. That is, there were in proportion to the population more than five times as many deaths recorded from cancer in 1912 as in 1840.

The fifth column shows the number of population in which there was an average of 1 cancer death recorded in the different years. In 1840 there was 1 recorded death from cancer, in the average, among every 5646

population; in 1912, 1 cancer death recorded to every 980 population.

The sixth column shows the proportion of cancer deaths to those that occurred from all causes. In 1840 there was 1 recorded death from cancer in 129 deaths from all causes; in 1912 the proportion was 1 to 13.

These figures for England and Wales are similar to those in the United States, but show a greater frequency of cancer. In the United States registration area in 1912, there was recorded on the average 1 death from cancer in every 18 deaths from all causes and 1 death from cancer to every 1299 of population in that area. Deaths from cancer under the age of thirty years are rare. In the United States registration area in 1912, of the recorded deaths over the age of thirty years, 1 in 11.5 was from cancer; of those over forty years of age, 1 in every 10.5 was from cancer.

The increase in cancer deaths is shown by the mortality records of every country in which such records are kept. The increase is not only universal for all countries but is also practically for all organs.

That there is an increase in the recorded death rate from cancer, as shown by the statistics quoted, is beyond question, and is accepted by all. That there is a real increase in cancer, and not merely an apparent one, is not so universally believed. There are two objections that are ordinarily made to the evidence of mortality records covering a period of years that cancer is increasing. One is that the number of correct diagnoses of cancer is increasing constantly, and the other is that the average duration of life is longer and a larger number of people live to the cancer age.

More accurate diagnoses are undoubtedly made at present than in 1840. These errors in diagnosis, however, were both positive and negative. Benign tumors were diagnosed as cancers, and malignant growths were not recognized as such. One error, at least, in part counterbalanced the other.

While there has been a great improvement in diagnoses between 1840 and the present, there has probably been little or none during the past five years to explain the increase of this more recent period. Furthermore, the diagnosis of cancer at the terminal stage, which is the stage at which the diagnosis for the mortality statistics is made, is not difficult, and in communities such as England and Wales it was probably made with as great accuracy in the past as at present. At present, early diagnoses are made with greater accuracy, but this improvement is not so evident for terminal conditions.

The diagnosis of the terminal stage of cancer of an accessible organ such, for example, as the breast, is so easy that those made in the past can hardly be questioned. Hoffman found that cancer of the breast in Rhode Island from the period 1876–1880 to that of 1896–1900 had increased 115 per cent. Also in Philadelphia, from the period 1861–1865 to that of 1896–1900, cancer of the breast increased 179 per cent. It is impossible to explain this increase in cancer of an accessible organ in any considerable part by mistaken diagnoses. The periods covered are too recent and the diagnosis too easy.

It must be accepted in general that more accurate diagnoses can explain only a small part, if any, of the increase in the recorded cancer death rate.

The increased average duration of life is a factor of influence in the increase of cancer. Beyond question, if a larger number of people live to the cancer age, more of them will develop cancer. Statistics show that the increased average duration of life is due largely to preventing the deaths of infants and young children, and that the frequency of deaths for later age periods remains practically the same as in years past. It has been shown that for these later age periods the percentage of cancer deaths is constantly increasing. That is, there has been a constantly increasing percentage of deaths from cancer among people of the cancer age.

This excludes the longer duration of life as an explanation of the increased recorded cancer death rate.

The influence of the modern treatment of cancer must have an effect on mortality statistics in the opposite direction to that for which better diagnoses and longer lives are urged. Unfortunately, the percentage of cancers that are cured is small, but in the aggregate they constitute a large number and would increase the number of cancers recorded.

Correct statistics on cancer deaths are probably also affected by the tendency still existing for physicians not to sign cancer as a cause of death. To many, cancer is considered a loathsome disease, one which places a stigma on the family, and the physician assists in its concealment.

There are other facts in regard to cancer, which are clinical and not entirely statistical, which add evidence to the increase of cancer. There is ample clinical evidence that cancer is rare among uncivilized people, and as they depart from their primitive mode of living, cancer appears and soon rapidly increases. An excellent example of this is given elsewhere in the description of cancer in Australia. The world is becoming more and more civilized, that is, it is departing more and more from a primitive mode of living, and if civilization increases the frequency of cancer, as is generally believed, then of course cancer must be on the increase.

The departure from a primitive mode of living is relative. The change in the mode of living from savage to civilized life among the aborigines in Australia is no greater than has taken place in the last two generations of civilized Europe and America. The increased wealth, the trend toward the city life, with less exercise, overeating, indoor life, etc., of the past two generations has made relatively greater changes among civilized people than has occurred from other causes among uncivilized races, and these changes undoubtedly account for at least a part of the increased cancer death rate.

A specific example which is caused by these changes, and about which there can be no doubt, is carcinoma of the stomach. There is no clinical doubt that gastric ulcer results frequently from overeating associated with worry and an indoor, inactive life, conditions of modern civilized city life, nor that gastric ulcer in a certain percentage of cases becomes a gastric cancer.

Carcinoma of the stomach is a frequent form of cancer and constitutes an important percentage of the total cancer cases. If it is caused by a gastric ulcer which is the result of modern eating and living, of which clinically there is no doubt, then it must be accepted that it is increasing.

Similar evidence exists for gall-bladder, the intestines, and other organs.

Taking all the evidence for and against the increase in cancer, it must be accepted not only that it is increasing but that it is doing so very rapidly. Also that the frequency of cancer is greater than mortality statistics indicate.

There is evidence that the increase in the death rate from cancer is more rapid in men than in women.

Theories of Cancer.—While the cause of cancer is unknown, there are various theories in regard to it, though none of them are entirely satisfactory in explaining all the known facts in regard to it. They assist, however, in giving a clearer conception of the cancer process.

Cohnheim's Theory.—This is based on the theoretical existence of misplaced embryonal cells. There are many examples of congenital defects and malformations in the formation of the body, such, for instance, as bronchial clefts, undescended testes, moles, nevi, etc. It is known that these congenital malformations are prone to undergo malignant change.

Cohnheim believed, just as there are macroscopic malformations, so also, in the formation of the different kinds of tissues, there are microscopic malformations in

the form of displaced cells in which cancer subsequently develops.

As malignant tumors do not usually develop until mature years, it is necessary to give explanation of this period of quiescence. It is known that certain senile changes occur in the tissues with advancing years. These changes occur earlier in some organs than in others. After the menopause, the breast and uterus, having completed their functions, begin a retrogressive process and it is at this period that carcinoma is most common in these organs. These same or similar changes occur at earlier periods from various causes, such as chronic inflammation, scar tissue, injuries, etc.

It is believed that the period of quiescence is caused by the growth of these displaced embryonal cells of Cohnheim's hypothesis being held in check and prevented from increasing by the control of the surrounding tissue cells. If this control is disturbed by the tissue changes of age, inflammation, irritation, etc., the growth of the displaced embryonal cells, no longer held in check, form the malignant growth. Once the malignant growth has started, it can be controlled no longer, and the ordinary clinical picture of a malignant growth is soon seen.

The hypothesis of Cohnheim will explain some of the facts in regard to cancer, but it has weak points.

That there were displaced embryonal cells at the point at which the cancer started is necessarily entirely theoretical. No one has ever actually seen the beginning of a carcinoma in such cells.

Cohnheim's theory of displaced cells does not explain the frequent development of cancer in scars, *x*-ray burns, chronic inflammations, etc.

In addition to the displaced embryonal cells, the existence of which is theoretical, it is, in Cohnheim's theory, necessary to have also some excitant, such as chronic inflammation, irritation, etc., to cause the malignant growth to develop.

Ribbert's Hypothesis.—Ribbert accepted the idea of displaced cells as a cause for cancer but did not believe that the displacement was necessarily of congenital origin. He believed that, as a result of irritation, interference with wound healing, etc., that tissue cells may become displaced, and that under some conditions, the growth of these displaced cells is held in check, but in other cases, on account of diminished resistance, these cells grow and proliferate and the malignant tumor is the result. Ribbert's theory is an extension of Cohnheim's, to include not only displaced embryonal cells but all displaced cells, whether from developmental processes or from accidental disturbances of postfetal life.

It is believed that the intitial change is not in the epithelial cells but in the connective tissue. As a result of inflammation, trauma, etc., there is a hyperplasia of the connective tissue which leads to the separation of epithelial cells from their original organic connection and also from the control with which they were associated. The removal of this control allows the abnormal growth of the epithelial cells, which is the malignant tumor.

Parasitic Theory.—Neither Cohnheim's theory nor Ribbert's modification of it gives a real exciting cause for the development of the malignant growth. They both describe theoretical cells, which are believed to change from a benign or dormant condition to a malignant one, but they do not give the cause of the change.

The parasitic theory supplies this exciting cause by the supposition that malignant growths are caused by living microörganisms. This theory, however, is now held by few scientists. Bacteria have been found in and about malignant growths, but there is insufficient evidence that they were concerned in the formation of the tumor. Certain bodies have been found in and between tumor cells and for a time it was believed by some that they were living organisms and that they were concerned in the development of the growth. It is now generally held that these bodies are not living organisms, and that

they have nothing to do with the formation of the growth. These bodies in most cases are probably natural products of the growth or of the degeneration of the cells themselves or of their nuclei.

There have been no organisms found that have been accepted by pathologists in general as the cause of cancer. The various bodies that have been reported as living organisms and the probable cause of cancer have been subsequently proved to be something else.

Recently, Rous has discovered a filterable agent which causes a spindle-cell sarcoma in chickens. This at least suggests that there is a definite virus for this particular tumor. It is possible that it may be produced by a microörganism.

The absence of microscopic and laboratory proof of the parasitic nature of cancer has forced the believers in this theory to clinical experience for evidence to prove the theory. This evidence has been insufficient. It is based on the possible infectiousness of cancer, as shown by cases of *cancer à deux*, cancer houses, streets, districts, etc. As stated in the section on infectiousness of cancer, all these conditions can be explained in other ways and there is little or no evidence that cancer is contagious.

It is possible that in the future, a parasite or living organism will be found to be the cause of cancer. The discovery of the cause of syphilis, and the resemblance of cancer in some respects to this disease, has made this seem more probable to some observers.

Up to the present time, however, that cancer is caused by a microörganism is a theory only and not an established fact.

CAUSE OF CANCER.

The real cause of cancer is still one of the unsolved problems of scientific medicine. The great frequency of the disease, effecting people of all classes in all civilized countries has directed the attention of the laity, the pro-

fession and even governments to the great importance of solving this problem. In all parts of the world there are well-equipped laboratories searching for the cause.

While the real cause has not been discovered, there are many facts that are well known to the men in the profession who have directed their attention to the study of cancer. It is possible that a more extended knowledge of these facts, and the proper attention to them, would be of as great service to humanity as the discovery of the cause itself.

Chemical Irritation.—There are a number of irritating substances which, by constant contact with parts of the body (for example, the hands of workmen), have a definite influence in the production of cancer. The irritation first produces a lesion, usually an ulceration, which is not malignant, but later, as a result of continued irritation, takes on a cancerous quality. The most frequent irritation in this class is soot and other products of the combustion of coal, guano, lead, tar, paraffin, aniline dyes, creosote, etc. Workers in these substances develop sores on their hands or elsewhere which are the starting-points of cancerous growths.

Soot.—As early as 1775 Pott described an ulcerative process which was common on the scrotum of chimney sweepers, and which he designated as "chimney-sweepers' cancer." The most typical and classical location of this growth is the under side of the scrotum, but a similar condition caused by the irritation of soot occurs on the face and hands, in fact, anywhere that there may be the continued irritation of the soot. For example, on the hands and face of men who work in the soot, or at furnaces or in coal mines.

The typical "chimney-sweepers' cancer" begins in the lower and posterior surface of the scrotum. At first it is an ulceration limited to the scrotum and is not unlike a syphilitic condition. Later it ulcerates more deeply and may involve the testicle, and then works upward along the spermatic cord to the abdominal cavity. The

inguinal glands may be involved. The growth is slow and, as the condition is of a low grade of malignancy, its early removal ordinarily resulted in a cure of the condition. In some cases the removal of one or both testes was necessary, in others the removal of a part of the scrotum was sufficient.

The disease probably was more frequent in America and England than in Germany due, it was suggested, to burning coal in the former countries, while wood is more generally burned in the latter. This would indicate that the soot from burning coal was a more active agent in the causation of cancer than the soot from the combustion of wood. One of the names used to designate the condition was "cancer anthracine."

At present the disease is rarely or never seen. More modern methods are used in cleaning chimneys, and greater care in regard to cleanliness, removes the soot and prevents the irritation from it. Finally, if an ulcer results as a result of irritation from soot, its possible significance is more generally recognized and proper means are taken to bring about its immediate cure. It is cured before it reaches the cancerous stage.

Tar and Paraffin.—In the process of distillation for the purification of tar and paraffin, irritated conditions of the skin are produced, which in some cases later develop into cancer. The condition of the skin is caused partly by the irritation of the substance itself and partly by the temperature to which it is raised. It is probable that the oily condition of the clothing is also an influencing factor.

There is at first an acute eczema with more or less discharge and, later, a chronic hyperplasia with the formation of horny outgrowths or warts which may be discolored. On this benign condition by further irritation the malignant growth may later develop.

The most frequent locations for the condition resulting from tar and paraffin irritations are the scrotum and the arms. There is a marked predisposition to the disease in some people. Some men go for years without showing

any irritation from work in these substances, while others are more susceptible and can work but a short time without developing the first signs of the disease.

There is no question that absence of cleanliness is an important factor in causing the disease. At present, on account of better hygienic care of the workmen, the disease is less frequently seen.

The course of the disease is slow, metastases are formed only late, if at all, and the removal of the growth usually effects a cure.

Tobacco.—Smoking of tobacco has long been considered an important factor in the production of cancer of the lip and of the tongue. Formerly the influence of smoking as a cause of cancer of the lip was assigned to the irritation of the stem of a clay pipe. While this is still considered a factor, the chemical irritation of the hot tobacco smoke, that is, of the products of combustion of the tobacco, is probably the more important factor, especially in carcinoma of the tongue.

Here, again, there is produced first a lesion which is not cancerous. It is at this early stage that the disease should be treated. By ceasing to smoke the benign lesion will usually heal, while if the smoking is continued, the benign lesion may become malignant. If this benign lesion on the lip or tongue does not heal by the cessation of smoking, then it should be removed, as the sure way of preventing its changing its character and becoming a malignant growth. The work of Bloodgood has shown how universally successful is the treatment of these cases at this stage.

The removal of such a lesion can be accomplished easily under a local anesthestic with little or no remaining deformity.

Physical Irritation.—The two most interesting agents in the production of cancer, through physical irritations, are the weather and *x*-rays. As in the case of the carcinomata which develop as a result of chemical irritation from soot, tar, paraffin, etc., there is produced first an

irritation of the skin, a benign lesion, which later changes to or has developed a malignant character.

Weather.—The skin of the face and hands of people who are constantly exposed to varying weather conditions has a thin, dry appearance, resembling that of advanced age. This is seen particularly in sailors, farm workers, etc., who are constantly out of doors in all conditions of the weather. By some it is described largely to the action of the sun's rays. More likely it is the result of the extremes of weather to which such people are exposed. The extreme heat and sun's rays during the summer and equally the wind, driving rain, sleet and possible freezing of winter, are the probable causes of this condition of the skin.

In these cases there is apparently a hyperemia of the skin with telangiectases and aggregations of dilated capillaries. There may be a deposit of pigment. Later there is an atrophy of the connective tissue and a hypertrophy of the epithelial layers. The thickened epithelium in places may fall off, leaving a small ulcer. This ulcer may be benign and easily healed or it may be the beginning of a malignant growth. The condition produced is very similar to xeroderma pigmentosum, a disease which also frequently leads to the formation of a carcinoma of the skin.

The progress of the disease is slow, there are usually no metastases, and the removal of the growth or its destruction with a proper cauterizing agent leads to a permanent cure.

Röntgen Rays.—The carcinoma of the skin which results from the action of *x*-rays is of special interest, as there can be no doubt as to the cause and effect. The connection is so absolute that there can be no doubt that the cancer of the skin is the result of the *x*-rays. This proves conclusively that certain forms of cancer, at least, are the result of irritation.

According to Wolff, the first observation of a cancer developing as the result of *x*-rays was published by

Freiben in 1902. A man, aged thirty-three years, as a result of *x*-rays, developed an ulcer on the back of the hand. This ulcer was at first apparently benign but later became malignant and necessitated an amputation of the arm.

As a result of the prolonged action of the *x*-rays, a dermatitis is produced, and later an ulceration develops. This ulcer may become malignant. In some cases, the malignant condition develops after the chronic dermatitis has existed for some time.

Chronic Inflammation and Ulceration.—There are in the literature various examples of cancers which are believed to have resulted from chronic inflammation. In some cases it is difficult to separate the influence of the chronic inflammation and that of other causes acting at the same time. In lupus of the face, which is sometimes followed by cancer, in addition to the chronic inflammation and ulceration, there are also the scar tissue and the frequent small injuries, which are factors in the development of malignant growths, and it is not easy to determine which of these conditions exerts the greatest influence.

In the skin in addition to lupus, chronic eczema and psoriasis are common diseases which might be considered chronic inflammations, and are sometimes followed by cancer.

A more positive example of the influence of chronic inflammation is seen in the malignant tumors which develop in infected wounds. In Löwenstein's series, in practically no case did a cancer develop in an open wound which healed by primary union. In a number of cases, in which the wound became infected, and was a long time in healing, a carcinoma developed. Under these conditions the chronic inflammation must be considered the exciting cause of the malignant growth.

Another example of the influence of chronic inflammation in producing a cancer of the skin is seen in old sinuses, chronic ulcers, etc. A number of cases of carcinoma

developing in old sinuses, both in the soft parts and those leading to bones, are reported in the literature. The same is true of chronic ulcers. A chronic ulcer frequently existed previous to the formation of a carcinoma of the leg.

On the tongue, lips, and cheeks an ulceration frequently precedes the development of an epithelioma. This has been described elsewhere.

In the stomach and intestines the most frequent examples of carcinoma following an ulceration are seen. The high percentage of gastric carcinoma at the Mayo Clinic, that were believed to have been preceded by an ulceration, is given in the chapter on Carcinoma of the Stomach.

In the Fallopian tubes carcinoma is rare, but chronic inflammation seems to be an undoubted influence in the cases reported. Martin, Kleinhaus and others have called attention to the importance of chronic inflammation in these cases.

In the uterus, carcinoma of the fundus may be the result of a chronic inflammation, though the evidence is not definite. Carcinoma of the cervix uteri, however, seems beyond question to be influenced by the chronic inflammation and the ulcerations or erosions which so frequently accompany it.

In these various examples of carcinomata that have developed in organs that have long been inflamed or ulcerated, there usually have been other influences at work which may have been of equal or greater importance. In the cheek, the continued irritation of the teeth and in the entire gastro-intestinal tract the irritation of an ulceration by food and intestinal contents may have been more influential than the chronic inflammation and ulceration themselves.

It is probable that the real influence of chronic inflammation and ulceration is partly in changing the tissues so that they are more disposed to malignant disease, and partly that the ulceration itself acts as an irritant.

Theilhaber believes that, as a result of the chronic

inflammation, an anemia of the mesodermal tissues is produced, resulting in a local condition similar to the general senile condition of tissues later in life, and in which cancer is known to be more apt to develop. The reason why cancer is disposed to develop in this senile tissue is not yet known.

In regard to ulceration, the influence is probably comparable to a chronic irritation. The ulceration is more delicate and more easily injured than the normal tissue in which it is located. The repeated small injuries may be the exciting cause of the malignant change. In a hollow viscus, such as the stomach, bladder, intestine, etc., the ulceration with the surrounding inflammatory induration, will not contract and expand with the same uniformity as the surrounding normal tissue. This will keep up a continual irritation of the ulceration, particularly at the edge, the point where the malignant change usually starts.

Trauma.—It cannot be stated with absolute certainty that there is any relationship between traumatism (that is, of a single injury, and not small, frequently repeated injuries), which would better be considered a chronic irritation, and a malignant growth. There is, however, ample clinical evidence that both sarcomata and carcinomata follow single injuries.

Williams apparently does not consider that the influence of trauma is as great as generally believed. Against its influence he urges the greater frequency of cancer among women, and mentions as an extreme example that mammary cancer occurs in the proportion of 1 male to 116 females. To the advocates of trauma as a cause of cancer, the comparison of the male breast with that of the female is not strong.

Williams also urges against the influence of injuries as a cause of cancer, the fact that in the parts where injuries are most frequent, for example, the extremities, cancer is most infrequent, also that while injuries are frequently multiple, primary cancers are rarely so.

Williams, however, recognizes that traumatism is a factor in cancer etiology, and expresses its influence as "spark in contact with combustible material."

Löwenstein published a series of 271 cases from the literature of malignant tumors which followed injuries. This series is by no means complete, nor does it correctly represent the frequency with which malignant growths are supposed to follow injuries, as most surgeons have seen a number of cases of cancer which seem to be the result of trauma. The series, however, well illustrates several points in regard to malignant growths resulting from injury.

In the series, 206 cases, or 76 per cent., were males, and only 65, or 24 per cent., were females. Williams found that fatal injuries in men are 2.8 times more frequent than in women. It is interesting that malignant tumors, which were supposed to be the result of injuries, should be three times as frequent in men as in women, when it is remembered that cancer in general is more frequent in females. That is, while cancers are more common in women than in men, cancers that were believed to result from injuries were more frequent in men than in women, and in about the same proportion that injuries are more frequent in men than in women. This can be considered as confirmatory evidence that the cancers resulted from injuries.

The variety of tumor which results from injury most frequently is sarcoma, though in general carcinomata are more frequent than sarcomata. In the series of Löwenstein, 221 cases, or 81 per cent., were sarcomata, and 50, or 10 per cent., were carcinomata. If the 26 cases of cancer of the skin, of which 16 cases were carcinomata and 10 cases sarcomata are excluded, 90 per cent. of the cases in the series were sarcomata, showing the much greater frequency with which this variety of tumor results from injury.

The interval of time that elapsed between the injury and the development of each variety of tumor is shown for Löwenstein's series by the following table:

Interval.	Sarcoma.		Carcinoma.	
Under 3 months . .	72 cases	34 per cent.	4 cases	8 per cent.
3 to 6 " . .	56 "	25 "	13 "	26 "
6 to 12 " . .	50 "	21 "	8 "	16 "
1 to 2 years . . .	29 "	14 "	14 "	28 "
2 to 3 " . . .	12 "	5 "	4 "	8 "
Later than 3 years .	2 "	1 "	7 "	15 "

The table shows that sarcomata develop more quickly after an injury than carcinomata. During the first three months, 34 per cent. of the sarcomata developed and only 8 per cent. of the carcinomata; within the first year 80 per cent. of the sarcomata and only 50 per cent. of the carcinomata had developed; after three years, only 1 per cent. of the sarcomata but 15 per cent. of the carcinomata developed.

The shortest interval between the trauma in Löwenstein's series and the development of a sarcoma was fourteen days. The history of this case, the location of the tumor in the scrotum, and the subsequent recurrence would all seem to exclude the probability of error in the observation. It is probable in some cases that the injury directed attention to a preëxisting malignant growth. For example, a case is reported of a carcinoma of the pylorus which was diagnosed five weeks after an injury and which died ten weeks later. Such a case certainly suggests that the growth existed previous to the injury.

Of the organs effected by cancer resulting from an injury, the bones are the most frequently involved. In Löwenstein's series, the bones were involved in 155, or 57 per cent., of all cases, and of these 108, or 40 per cent., of all cases were in the extremities. The bones, particularly those of the extremities, are the parts most frequently injured and are also most frequently involved in sarcomata, the most common type of post-traumatic cancers. It is natural, therefore, that the largest percentage of the cases should be found in the bones.

The testis is also frequently injured, and frequently the seat of sarcoma. In Löwenstein's series it was

involved in 22 cases (21 sarcomata and 1 carcinoma), or 8 per cent., of all cases.

The female breast, from its location, is frequently injured, and naturally one would expect it to be involved in a post-traumatic lesion. In Löwenstein's series it was involved only 9 times. It is noticeable that of these 9 cases, 4 cases were sarcomata and 5 cases carcinomata, which is a much larger proportion of sarcomata than is found among malignant disease of the breast from all causes.

Of the uterus, Löwenstein does not include any cases. The trauma of childbirth is usually considered to be one of the important causes of cancer of the cervix uteri, and the fact that carcinoma of the cervix uteri is rare in nulliparæ, that is, in cervices which have not been injured, supports this view.

The nature of the injury is an important factor in the development of a post-traumatic cancer. An incised wound that heals primarily is rarely followed by a cancer. Occasionally, as described elsewhere, a cancer may develop in the scar and it is usually of the carcinomatous variety. In Löwenstein's series, there was practically no case reported in which a cancer followed an incised wound which healed by primary union. If an incised wound became infected, healed slowly or ulcerated, a cancer sometimes resulted. The wound that resulted from an ulceration, a bite, or a contusion, was the more frequent type of open wound that caused a cancer in the series.

The most frequent injury that causes a malignant growth is a contusion such as results from a kick, blow, fall, etc., and not the open wound. A cancer may also follow a strain such as may result from overlifting, slipping, or spraining a joint.

Usually the injury is slight or at least not extensive. For example, of 35 cases of post-traumatic cancer of the bones of the upper extremities, in Löwenstein's series, there was a fracture apparently only in 3 cases.

Injuries seem to act directly and indirectly in the production of cancer. In some cases the malignant growth develops shortly after an injury, usually of a subcutaneous variety, and the malignant growth seems to be the direct result of the traumatism. This direct influence of an injury in the development of a cancer is illustrated by the formation of a sarcoma of the testis from a contusion without external wound and within a few weeks. In other cases, the malignant growth is the indirect result of the injury. The injury causes a wound which becomes infected or ulcerates, and the malignant growth is the result of the inflammation or ulceration. That is, the cancer seems to be caused by the chronic inflammation or ulceration rather than the direct result of the injury. This direct influence of a trauma is seen in an open wound that is infected and fails to heal, such as a bite in the cheek or a lacerated wound on the skin.

Another indirect way in which a trauma may cause a malignant growth is through the formation of scar tissue, which, through irritation or in some unknown way, influences the formation of a malignant growth. An example of this influence of an injury is often seen in the breast. A carcinoma or sarcoma may develop in the breast at a point where a contusion was received one, two or more years previously and during which interval there had been no palpable change or only a slight hardening in the breast. The explanation of a case of this kind is that the injury produced subcutaneous scar tissue which acted the same as similar tissue resulting from a mastitis or other cause.

PREDISPOSITION TO CANCER.

It is not easy to determine to what extent there is an individual predisposition to cancer. It is generally accepted that some people possess a definite predisposition to certain diseases. Under apparently similar conditions some people will contract a disease while others will

escape. This may be due to a greater predisposition to the disease possessed by those who contracted the disease or to a greater immunity possessed by those who resisted it. This immunity may be artificially acquired, as by vaccination against smallpox or the use of anti-typhoid vaccine, or it may be acquired as the result of a previous attack of the same disease.

There is some evidence that this is also true of cancer, that is, that some people are more liable to the disease than others. Among animals there is positive evidence that some are more susceptible than others to cancerous growths. For example, rats and mice, and of these certain species show an undoubted predisposition to malignant growths. Of the nature of this disposition little or nothing is known. Attempts have been made experimentally to immunize animals against the implantation of cancer cells.

Among humans everyone accepts that there is greater disposition to cancer in middle and old age. This disposition, however, is for the entire race and not for individuals. The influence of sex and heredity are subject to differences of opinion.

There is no doubt of the greater susceptibility of some people to certain precancerous lesions, such as chronic eczema, irritation of skin from soot, tar, etc. In this indirect manner, such people might be considered as predisposed to skin cancer.

Age.—A malignant tumor may occur at any age. It may even be congenital. They occur with increasing frequency, after the first five years, up to seventy-five or eighty years of age, and according to some observers up to the oldest age reached by man. That is, for the same number of people living at a certain age after five years, the greater will be the number of deaths from cancer, the older that age is up to eighty years, when possibly the number will be smaller.

In order to get correctly the age incident of cancer, the number of deaths from cancer during an age period,

and also the number of people living at that period, must be considered. There are absolutely more deaths between the ages of forty and fifty years than between sixty and seventy years, and there are many more people living in the former age period. There is, however, a greater percentage of deaths from cancer in the latter period. The death rate per 10,000 population for different ages and age periods is illustrated by the following table computed from the mortality records of Prussia. Of every 10,000 living there died of cancer in 1898, in Prussia:

Age.	Males.	Females.
Under 1 year	0.46	0.43
1 to 2 years	0.18	0.23
2 to 3 "	0.30	0.28
3 to 5 "	0.27	0.27
5 to 10 "	0.14	0.09
10 to 15 "	0.11	0.13
15 to 20 "	0.26	0.19
20 to 25 "	0.33	0.45
25 to 30 "	0.57	0.86
30 to 40 "	1.84	3.02
40 to 50 "	7.89	11.05
50 to 60 "	20.70	21.37
60 to 70 "	39.46	32.52
70 to 80 "	36.52	34.24
Over 80 "	26.30	26.87

It will be noticed in this table, which is representative of others showing the same thing, that there is a moderate decrease in the number of deaths from malignant tumors from birth to the fifth year. This same thing is shown in the mortality statistics of the United States Census Bureau in which more deaths are recorded from malignant growths during the first five years than for any other five-year period until after the twentieth year. This is doubtless due to the deaths from malignant growths which were congenital or resulted from congenital defects.

It will be noticed also that after the fifth year there is only a slight increase for each age period until thirty years of age, when there is a much more rapid increase to seventy years for men and eighty years for women,

at which ages there is again a decrease in the death rate. Some observers do not record this final decrease in the death rate, but believe that it continues to rise with the increasing age. This final decrease in the cancer death rate might be explained by greater care in eating, mode of living and freedom from accidents, irritations, etc., which might offset the greater disposition to malignant growths of the more senile tissues.

It will also be noticed that between the ages of thirty and sixty years there is a larger percentage of deaths among women, and between sixty and eighty years it is larger among men.

As has been shown by the table quoted, malignant tumors may occur at any age. The malignant tumors that occur before the twentieth year are practically all sarcomata. Carcinomata are rare before that age. Of 942 malignant tumors seen by Williams, 806 were carcinomata and 136 were sarcomata. Of the carcinomata, only one case originated under twenty years of age. Of the 136 sarcomata cases, 24, or 17.5 per cent., were under twenty years of age at the onset of the disease.

Of 1789 cases of sarcoma reported by Williams from mortality records, 261 cases, or 14.6 per cent., were under twenty years of age at the time of death.

Sarcomata may occur at any age and frequently are congenital, but carcinomata are rare before twenty years of age.

According to Williams, the earliest authentic case of a malignant epithelial growth was in a girl, aged eleven years, who had a cylindric-celled carcinoma of the rectum.

The oldest patient known to Williams, who died of a malignant tumor, had a cancer of the eye and one of the wrist, and died at the age of one hundred and six years.

Sex.—Sex exerts a great influence in the incidence of malignant growths, largely due to the frequent occurrence of cancer in the female breast and the uterus and the infrequent occurrence in the corresponding male organs. The greater frequency of malignant growths in females applies

to carcinomata but not to sarcomata. For example, of 1350 cases of sarcomata of different organs studied by Williams, 702 cases occurred in males and 648 cases in females. In 1912 in England and Wales the death rate from cancer was 91 per 100,000 males and 117 per 100,000 females.

In the United States in 1912, assuming that the rate for the entire country was the same as in the registration area, in a total of 73,611 deaths from malignant tumors, 29,202 were in males and 44,409 in females. The sex ratio was therefore about 1 male to 1.5 females, or 50 per cent. more females than males.

According to Williams, cancer deaths are increasing more rapidly in males than in females, and there is therefore a decrease in the sex ratio. As determined by him, presumable for England and Wales, the sex ratio was for the period 1851 to 1860, 1 male to 2.2 females, 1881 to 1890, 1 male to 1.7 females and from 1901 to 1905, 1 male to 1.3 females.

Williams believes that the greater increase in the cancer death rate of males is due to more of them living in cities and their lives more closely resembling those of women, that is, more indoors, less exercise and greater indulgence in food.

Heredity.—There are wide differences of opinion regarding the influence that heredity may play in the development of cancer. The earliest writers considered that cancer was hereditary, but of more recent years there have been two schools, one holding that cancer is hereditary and the other that it is not. Most observers hold that the influence of heredity is a small one, if it exists at all.

A strong argument, to those who believe that cancer is hereditary, is the existence of "cancer families." In these families, members in different generations develop cancer in larger numbers than would be expected from chance. The existence of such families, though not frequent, are undoubted. To those who believe that

cancer is hereditary, these families are usually considered as evidence of such an influence. Those who do not believe that cancer is hereditary explain "cancer families" by chance.

The most noted "cancer family" is that of Napoleon. Napoleon's father, he himself, a brother, and two sisters all died of cancer.

The most extensive "cancer family" is the one reported by Broca, in 1866, and quoted by Wolff and by Williams. In this family Madame Z. died of cancer of the breast. She had four daughters, two of whom died of cancer of the liver and two of cancer of the breast. In the third generation of five males and thirteen females, one male and nine females died of cancer. Of this family, Madame Z. and twenty-two descendants, eighteen died of cancer and five did not.

It is possible that cancer families, as claimed by some, can be explained by chance. Granting, however, that they cannot be, and that they are evidence of the transmission of cancer by inheritance, then it must also be accepted that they show that the influence of heredity is a small one. The number of "cancer families" compared with the enormous number of cases of cancer, is small, much smaller than would be the case if heredity played an influential part in the origin of cancer.

It would seem that the occurrence of cancer families could be explained better by chance than by heredity.

Another influence in the development of cancer, which in a way is hereditary, is seen in certain skin conditions such as nevi, warts, moles, etc. It is generally accepted that these conditions show an hereditary tendency. It is also known that they may become malignant. The hereditary influence in these conditions is an indirect one. The most that can be claimed is that a lesion which has certain cancerous tendencies was inherited, and not the cancer itself.

In the same category are cases of carcinoma of the skin, in which several members of the same family are

diseased. Wolff refers to a family reported by Rüder, in which seven boys between the ages of five months and ten years, all of whom developed epithelial carcinomata of the skin. In these cases, as with the nevi, moles, etc., it is probable that a skin lesion which possessed cancerous tendencies was inherited, and not the cancer.

Cases of this kind constitute a small part of all cancer cases and here, again, at most, heredity plays a small part.

The strongest argument against the inheritance of cancer is that the frequency with which cancer occurs can be explained by statistical evidence.

Of all people who pass the age of forty years at least one in twelve dies of cancer. As each person has two parents and four grandparents, two people together would have twelve direct ancestors in the two previous generations. As at least one person in twelve past the age of forty years dies of cancer, the chances are that of every two people who contract a cancer, one of them will have had a parent or a grandparent who had a cancer. In other words, the probabilities are that at least 50 per cent. of all cancer cases, in fact 50 per cent. of all people, will have a parent or a grandparent who had a cancer.

When the side lines are also considered, that is, the brothers and sisters, uncles and aunts, it is obvious that the chances are that every person has a near blood relative who had a cancer.

Additional valuable information on hereditary influence in the origin of cancer is obtained from mortality records of life insurance companies. Practically all who take out life insurance policies are people of intelligence, and the records are taken with more care than ordinary clinical histories. These life insurance statistics are therefore of great value in determining the influence of heredity in cancer.

A careful study of life insurance statistics has shown that the cases that die of cancer have a family history of cancer no more frequently than those who have died

of other diseases. If this observation is correct, and there seems to be every reason to consider it so, it is strong evidence against heredity as an influence in cancer.

If all the evidence for and against heredity as an influence in cancer is considered, the probable conclusions are:

1. That in most cases, heredity exerts no influence in cancer.
2. That there may be possibly an exception in this in some families.
3. That some precancerous lesions such as warts and nevi may be hereditary.

GEOGRAPHICAL DISTRIBUTION.

Climate.—There have been radical changes in the opinions of men regarding the influence of climate on the prevalence of cancer. At one time it was believed that the warm, moist climate of the tropics favored the development of the disease; later, the opposite opinion, that the cold of the north was more favorable to it. It is now known that cancer is found in all parts of the world, and it is believed that climate itself has little or no effect on its occurrence. There are other factors that are more influential in its occurrence in different countries. In the temperate regions there is an older and higher civilization, and it is this higher civilization, with all that it means in food, manner of living, housing, occupations, etc., and not climatic conditions, that is the cause of the higher cancer rate.

Race.—In regard to race, there is no doubt that there is a difference in the prevalence of cancer among different races or nationalities. While it is not possible to exclude the climate as an etiological factor, there are other causes that seem to exert greater influence. Apparently the lower the grade of civilization the more infrequent is cancer. It is probable that among primitive savages, such, for example, as those of Central Africa, cancer is

rare. There are, of course, no accurate statistics in regard to the cancer death rate among these uncivilized races, but the repeated observations of military surgeons and medical missionaries confirm this belief. As soon as the uncivilized races come under the influence of civilized life the cancer death rate increases. For example, as has been stated, malignant tumors among the races of Africa are believed to be rare; this was true of these people as slaves in the United States, but after the emancipation the cancer death rate increased and is now practically the same as that of the white race. As slaves their physical condition was carefully looked after, their work was largely out of doors, their food simple and not excessive, there was no overeating or drinking or general dissipation. It was to the interest of the owner to look after his property. After the slaves were freed, they deteriorated in physical condition as a result of dissipation, overeating and drinking, bad housing, constitutional diseases, etc. These changed conditions and the increased cancer death rates are known, and it is probable that one is influenced by the other.

The same conditions are seen in Australia, where a highly civilized white race is living under the same climatic, but different personal conditions, as a race recently and rapidly changing from a savage to a civilized people.

In an interesting paper, Allen compares the cancer death rate of Australia for 1900 with that for 1870, and found that the cancer death rate of both sexes had increased from 27.5 to 57.2 per 100,000, an increase of more than 100 per cent. Allen explained the increase in the frequency of cancer in Australia by the larger number of people living to the cancer age. This would doubtless explain a part of the increase, but not all of it. It is probably also due to the increased civilization of the native people, the greater accuracy of statistics and to the better opportunity of the natives to obtain hospital or medical attention. During 1900 in England and Wales the cancer death rate was 82.8 per 100,000. This would indicate that cancer

in 1900 was about 30 per cent. less frequent in Australia than in England and Wales. Allen believed cancer to be rare among the Australian aborigines, but that it is rapidly increasing among them.

Adams studied the cancer death rate of the native, and of the British and foreign-born population of Australia for the year 1900. According to Adams, the death rate for 1900 was 57.3 per 100,000 living inhabitants, and of this number 17.1 were native-born and 40.2 were British or foreign-born. Considering only the population over thirty-five years of age, the total death rate per 100,000 population was 195.3, of which 58.2 were native-born and 137.1 were British or foreign-born. Adams corrected these figures regarding the number of native, British and foreign-born inhabitants, and found that the cancer death rate for 100,000 native-born inhabitants over thirty-five years of age was 81.3 and for 100,000 British inhabitants over thirty-five years of age it was 490, and for 100,000 foreign-born over thirty-five years of age it was 351.6. These figures are of special interest, as they show the difference in cancer death rates of different races living under the same climatic conditions.

These statistics of Allen and Adams are here of definite value. Those of Allen would seem to indicate the increasing cancer death rate of a native people becoming civilized. The figures of Adams show the higher cancer death rate of the more highly civilized part of the population.

In Europe there is the highest, or perhaps better, the most luxurious civilization of any part of the world. The people are, as a whole, well nourished, most live in towns, many work indoors, and there is the highest cancer death rate.

According to Williams, the cancer rates per 100,000 population, about the year 1900, for different countries of Europe, were as follows: Switzerland, 132; Denmark, 130; France, 104; Sweden, 102; Holland, 93; Norway, 92; England and Wales, 82; Scotland, 61; Italy, 52; Spain, 39.

Williams explains the high cancer rate of Switzerland

and Denmark by the higher average general welfare of the people, that they have neither the very rich nor the very poor. He also calls attention to the general low death rate from cancer along the Mediterranean shores, as shown by statistics quoted.

There are so many factors that enter into cancer statistics that it is not possible to make absolute comparisons. That the recorded cancer death rates in Europe are higher than in other continents is beyond question, and it probably indicates that the higher the civilization and general welfare the greater the cancer death rate. Williams considers that this is the only explanation, and that it is not possible to explain it by age, sex, better diagnosis, etc. In the United States registration area in 1912 the cancer death rate was 77 per 100,000 population. This corresponds closely to the rate in European countries.

In Africa, except in limited areas inhabited largely by Europeans, there are no accurate cancer statistics. Information regarding cancer comes largely from medical missionaries and army surgeons, and consists of clinical impressions rather than statistics. They all practically agree, that among the native black races cancer is unknown or rare. For example, Madden states that the medical men in Egypt agree that cancer is not found among the black races in that country, but that it is fairly frequent among the Arabs. Forde did not see a case of malignant tumor among natives in nine years' practice in Gambia. Similar statements are recorded for the native population throughout Africa.

In South Africa, Williams states that cancer is fairly common among those who eat and live as Europeans. Among the natives who live a simpler, vegetarian life, cancer is rare.

Various causes have been offered for the infrequent occurrence of cancer among the black races of Africa. The protection offered by the pigment of the skin, the relative absence of smoking, the vegetable diet, and few

gastro-intestinal disturbances, the high infant mortality and the fewer people living to the cancer age, are all considered as possible influences.

Of the distribution of cancer in Asia, little is definitely known from careful statistics. It is generally believed that in China, cancer is fairly frequent, but apparently the number of cases is not large, and the information is based on the reports of medical missionaries and a few hospitals, and not from a survey of the entire country. In Japan, in 1905, the cancer death rate, according to Buday (Wolff), was 53 per 100,000 living inhabitants.

Cities and Country.—Even when corrected for age, sex, hospital facilities, and diagnosis there seems to be greater frequency of cancer in the inhabitants of cities than in the country. This is illustrated for France by the following rates for 1900 per 100,000 inhabitants as given by Williams:

Paris	121
Cities over 100,000 population	112
" 30,000 to 100,000 population	99
" 20,000 to 30,000 "	95
" 10,000 to 20,000 "	91
" 5,000 to 15,000 "	74
" under 5000 "	82

In Hungary, as reported by Dollinger, there is a much greater difference in the cancer death rate of cities and the surrounding country. For example, of the inhabitants of Budapest over fifteen years of age the rate, 1901–1904, was 121, while in the surrounding country it was only 59 per 100,000. In some localities the difference was even greater. Dollinger also quotes the rates for Denmark as follows:

Copenhagen	54
Other cities	47
Surrounding country	38

In Scotland there is a slightly greater frequency among those living in the country than in the cities. It should

be remembered, however, that in England and Scotland the difference between city and country life is not as marked as in some countries.

It is not possible to explain the reason for the greater frequency of cancer in the cities, excepting in general statements. There is a tendency for people after childhood to leave the country and go to the cities. This would mean that in 100,000 people living in the cities there would be a larger number of the cancer age than among the same number of country people. In large cities the hospital facilities are such that the people go there from the country for better care, and their deaths, if they occur, are recorded for the city. This is a factor of importance. The element of better diagnosis is one of less importance, because in the terminal stages the nature of a malignant growth is usually too evident to be mistaken by a practitioner of medicine.

LITERATURE.

Adams. Lancet, 1904, i, 422.
Allen. Australasian Med. Gazette, 1902.
Broca. Traite des Tumeurs, 1866, p. 151.
Forde. Report on Cancer in British Colonies, 1905.
Madden. British Med. Jour., 1902, ii, 730.
Milne. British Med. Jour., 1905, ii, 925.
Stern. Deutsch. med. Woch., xviii, S. 494.
Williams. British Med. Jour., 1890, ii, 895.

CHAPTER II.

PRECANCEROUS LESIONS.

The first use of the word precancerous was probably by Butlin about twenty-five years ago, when he applied it to certain lesions of the tongue which showed a particular predisposition to change from a benign to a malignant growth, and there are today no better examples of lesions to which the term precancerous can properly be applied than to these same tongue lesions. Of late the term is being more commonly used. This is due partly to the greater interest that has developed in regard to cancer, but probably more particularly to the greater willingness of pathologists to express the opinion that a certain lesion is not a cancer but is a type that is liable to become one. It is for such a condition that the term precancerous is needed.

The exact meaning of the expression should be understood. A precancerous lesion is not a cancerous lesion; it may not even become one. It is, however, a lesion of the type that is known to become cancerous in a larger percentage of cases than most benign lesions. The term is not exactly a scientific one, but it describes a definite condition for which there is no other concise expression.

It is of considerable practical importance that this condition should be described by some concise and expressive term, because by doing so a better understanding of these lesions and a more frequent recognition of their importance will be brought about.

It is possible by further advance in the pathology of malignant growths that it will be possible to determine more positively and more frequently what benign lesions

are liable to change their character and become malignant, and also the time when the change is taking place. This would add to the list of known precancerous lesions.

The operative treatment of malignant growths is not satisfactory, and the constant regret of surgeons is that cancer cases are seen too late. It is possible that in the future, by more frequent recognition and cure of precancerous lesions, much can be accomplished in the prevention of cancer and also in the earlier recognition of it.

The statistics of operation on precancerous lesions must not be confused with those performed for cancer. A precancerous lesion is not a cancer, and when removed it shows no tendency to recur or to form metastases. If it did, then it was not a precancerous but a cancerous lesion. The percentage of cures of precancerous lesions is effected only by the primary operative mortality.

The early recognition of precancerous lesions is of sufficient importance to group the most important ones together.

Tongue.—A frequent precancerous lesion of the tongue is leukoplakia, also known as chronic glossitis, leukoma, etc. This is a chronic condition which at first resembles the white mark produced by a stick of nitrate of silver.

There may at first be one or several white patches, which later unite and cover most of the dorsum of the tongue. At first the tongue is soft and pliable, but later, due to the thickening of the epithelium, it becomes more hard and rigid. If the superficial epithelium is scraped off there remains a red, bleeding ulcer on the tongue. The disease runs a chronic course and seems to yield to no treatment other than absolute destruction with the cautery.

The two important etiological factors usually given for leukoplakia are tobacco smoking and syphilis. The influence of the smoking is partly the burning and partly irritation of the products of combustion.

Leukoplakia is most frequently seen on the tongue, but cases are reported in which it has occurred on the penis,

lip, cheek, in the nose, larynx, bladder, vulva, and vagina. Wherever it occurs, it should be considered a lesion which is liable at any time to become cancerous, and it should be removed, destroyed with a cautery, or carefully watched for possible malignant change.

No positive cause for the malignant change that may occur in leukoplakia can be given. A condition is produced in the tongue by the leukoplakia that is easily injured by its normal movements, food, etc., producing small cracks and areas of chronic inflammation. These small, frequently repeated injuries and the chronic inflammation may exert the same influence in the tongue as elsewhere in the production of a malignant growth. It is possible that the thickened, superficial layer of epithelium may act as a foreign body and produce the malignant change by causing a chronic irritation of the more normal parts.

Any ulcer of the tongue which does not heal promptly should be considered a possible precancerous lesion. The most common ulceration of this kind is one that appears toward the tip of the tongue and is the result of smoking, that is, of being repeatedly burned by a hot pipe stem or irritated by the hot smoke.

Another ulceration on the tongue, which falls in this class, is one that may form at any place on the margin of the tongue from irritation of broken teeth, particularly if associated with syphilis and excessive smoking.

Obviously the cure of these lesions is the removal of the cause.

Cheeks.—Precancerous lesions of the same nature as the ulcerations which occur on the tongue may arise in the cheeks and on the gums. That is, there may be patches of leukoplakia, or ulcerations from smoking, broken teeth, etc. They are, however, of less frequent occurrence.

Lips.—While any chronic ulceration of the lip must be regarded with suspicion, the most important precancerous lesion of the lip is one which results from smoking and

is occasionally known as smoker's patch. It is caused by repeated irritation or burning of a hot pipe-stem or hot smoke. It may appear first as a small blister, or as a crack or fissure, or as a thickened or tanned area.

The work of Bloodgood has directed attention to the importance of these early lesions, and is of great value. He has shown that if removed at this stage they are all cured. It is probable that many would disappear if not removed; it is equally true that many would develop into malignant growths.

Skin.—A number of the chronic diseases of the skin are believed to influence the development of cancer. The connection is not a close one, and it is difficult to prove the direct relationship between the skin disease and the cancer. In many cases the skin disease has existed for years previous to the appearance of anything of a malignant nature, and it is probable that in many cases it is merely a coincidence that the two diseases occur in the same place.

Chronic eczema is probably more frequently followed by cancer than any other disease of the skin. Paget's disease of the nipple is frequently cited as an example of a malignant disease following a chronic eczema. In Paget's disease there is at first a lesion which has all the signs of a chronic eczema about the nipple. Later an ulceration is formed with involvement of the breast. Some observers, however, regard Paget's disease as malignant from the start and not related to a chronic eczema.

Two other special locations where chronic eczema is apparently followed by an epithelioma is about the scrotum and about the anus.

Lupus.—Lupus has long been regarded as a precancerous skin lesion. As early as the middle of the nineteenth century, cases of carcinoma developing on lupus as a base were reported.

The lesions of lupus possess a number of characteristics that are believed to predispose to the formation of cancer. There is an ulcer which is the seat of a chronic inflam-

mation. The ulcer heals in places, but the scar is an unhealthy one, and is frequently injured and breaks down to form a new ulceration. The unhealthy scar, the ulceration, and the chronic inflammation all predispose to cancer, and they are probably the influences that change the lupus to carcinoma.

The carcinoma that develops on lupus may originate in the scar or in the ulceration itself. Some writers designate two varieties: lupus carcinoma and lupus scar carcinoma, depending on the place in which the carcinoma originates.

Clinically, the carcinoma that develops on lupus is similar to other epitheliomata of the skin. It usually develops after the lupus has existed for a number of years, and in a patient who has reached the cancer age. The edges of the ulceration become hard and indurated. In the centre the growth extends into the deeper tissues, forming a more extensive ulceration. In rare cases a papillomatous form is reported.

Lupus vulgaris shows a greater disposition to become malignant than the other varieties of lupus.

Ulcers.—The relation of simple ulcers of the skin to carcinoma is not a close one. The most frequent location of chronic ulcers is on the lower extremities. Not only are ulcerations in that locality of common occurrence, but they are exposed to frequent injury, and they occur most frequently during the cancer age, yet carcinoma of the extremities is of rare occurrence. A number of cases, however, are reported in the literature in which simple ulcer of the leg after persisting for a number of years as a benign lesion has taken on a malignant change. The malignant change starts and progresses from a single point, the edges become raised and hard, and the centre may at first grow more exuberantly, but later breaks down, forming a deeper excavation.

While the number of cases of carcinoma of the lower extremities is small compared with the ulcers in that locality, the ulceration should be considered as a possible

etiological cause of the carcinoma. It is impossible to state the exact manner in which its influence is exerted. The influences which produce and retard the healing of the ulceration itself are probably also factors in the development of the carcinoma. The chronic eczema of the skin, the chronic edema due to varicose veins, and the frequent traumatism are the most important of these influences. It is probable, too, that the ulceration itself, associated as it always is with some chronic inflammation, may act as a constant irritant to the tissues, and this irritation may influence the development of carcinoma.

Closely resembling cutaneous ulcers in their influence on the development of cancer are old sinuses. According to Wolff, the tuberculous sinus and that associated with osteomyelitis are most apt to develop a malignant change. Wolff also refers to cases reported in the literature of either sarcoma or carcinoma developing in a fistula in ano, in a urethral fistula, and in the sinus resulting from a gunshot wound with retention of the bullet. None of these cases are frequent, but of all cases of epitheliomata of the extremities a large percentage of them develop in chronic ulcers.

Frequent examples of carcinomata developing in pre-existing simple ulcerations are seen in the stomach, and there is at present a free discussion among surgeons and pathologists in regard to the frequency with which this malignant change occurs in gastric ulcers. That such a change does occur there is ample clinical and laboratory proof, and no doubt is raised in regard to it. The frequency with which it occurs is more difficult to determine. At the Mayo Clinic it is reported from independent clinical and laboratory examinations that considerably over 50 per cent. of all cases of carcinoma of the stomach developed on a simple ulcer. This estimate is much higher than is generally accepted. Most surgeons estimate that between 5 and 25 per cent. of the gases of gastric cancer were preceded by an ulceration.

There are no statistics which give the frequency with

which a gastric ulcer changes from a benign to a malignant condition. These statistics would be difficult to obtain, but would be of great practical importance. There is no doubt that the number is only a small percentage of all cases of gastric ulcer.

There are several possible causes which influence the change of a gastric ulcer from a benign to a malignant lesion. As has been stated in regard to ulcers of the extremities, the gastric ulcer itself is associated with chronic inflammation which predisposes the tissues to malignant growth. In addition a gastric ulcer is subjected to the irritation, both physical and chemical, of food and stomach contents, and also to the movement of the organ.

Scars.—According to Wolff, the first published observation of a carcinoma developing in a scar was made by McPherson as early as 1844. There have since been many observations of carcinoma developing in scars and various theories advanced to explain them.

There are some scars which show little or no tendency to develop malignant change; there are others that show a marked tendency to do so.

The rupture of the hymen leaves a scar, but a carcinoma rarely develops in this location. In women who have borne children there are scars in the vagina, but carcinoma rarely follows. In this group there would also be included the scar of the penis following circumcision, of the ovaries following frequent rupture of Graafian follicles, of the hands of workmen following frequent injuries.

Carcinomata may occur in any of these, but only rarely in comparison with the frequency of the scars. These scars are all entirely healed, and might be termed healthy scars.

In the second group of scars, carcinomata develop more frequently. The first places in this group of scars are those which are the result of burns, particularly if the scar is located so that it is frequently injured. Another scar, probably of equal importance, is that of the

cervix uteri resulting from childbirth. In this group are included the scars of ulcers, particularly if not entirely healed, such as those of the leg or stomach, also mastitis, syphilis, and lupus. These scars are less healthy than those of the former group.

The period of time that elapses between the formation of the scar and the development of the carcinoma varies greatly. It may be only a short time, that is, a few months, but usually it is at least a few years and often twenty or more years. Cases in which a carcinoma develops in the scar of a wound for the removal of a malignant growth should not be considered in this class, as such cases are more probably the result of implantation of cancer cells at the time of the operation.

There are at least four theories or explanations of the development of a carcinoma in a scar.

The first theory is that in the healing of the wound that caused the scar, some of the hair or sebaceous follicles of the skin were covered over by epithelium in the cicatrization of the wound and their ducts obstructed. This prevented the discharge of their secretions, which then acted as an irritant and produced the carcinoma. According to this explanation, the carcinoma originates in the gland epithelium and then breaks down forming an ulceration.

Another theory which is advanced by Thielhaber is that in the lesion that produced the scar there was a destruction of tissues and a definite interference with the blood supply and the nutrition of the parts. This condition closely resembles the tissues of advanced age, in which carcinoma is disposed to occur. It is stated that as a result of this condition there is an overgrowth of the cellular structure, while the intercellular and fibrous tissue atrophies. This overgrowth of the cells results in the carcinoma.

Another theory is that the scar acts as a foreign body and irritates the surrounding tissues. This cicatrix, situated as it is in the tissue of different elasticity and

resiliency, does not yield freely, and as a result the tissues are irritated by it. According to this explanation the scar itself is the irritant.

Still another theory is that the scar is irritated or injured, and a carcinoma is started in the cicatrix as in any other place, excepting that the scar is abnormal and more easily injured, and therefore a cancer may be developed in it more easily than in normal tissue. There are various examples of carcinoma developing in a scar that has been directly irritated or repeatedly injured. This is most frequently seen in the scars resulting from burns. The scar from a burn is often thin and delicate and easily injured, particularly if it is in an exposed place. A slight injury may cause a small ulcer which heals slowly and often breaks out again after it has healed. If a cicatrix resulting from a burn, as on the flexor surface of an extremity and its contraction, has limited full extension it may be repeatedly injured by the ordinary movements of the arm or leg. If a carcinoma develops in a scar under any of these circumstances, it is probable that it was caused by irritation or repeated injuries.

None of these theories really explains the cause of the development of a carcinoma in a scar. They all describe certain phenomena that occur in connection with scars and carcinomata, but fail in demonstrating the real cause of the development of one in the other. There is no doubt that a carcinoma sometimes develops in a scar. Neither is there any doubt that the scar had a definite influence in the development of the malignant growth.

When the enormous number of small scars of various kinds and the infrequency of scar cancers are considered, it must be appreciated that the influence of a scar in the development of a malignant growth is small. It is possible, however, that a better knowledge of the etiology of malignant growths will show the influence of scar tissue. It has been shown that a previous history of acute mastitis is common in cases of carcinoma of the breast, and it is

probable that the scar tissue in the breast is the active factor. A better knowledge of the pathology of malignant growths may show the way in which scar tissue affects the malignant growths.

Benign Growths as Precancerous Lesions.—The change of a benign into a malignant tumor, that is, the so-called malignant transformation of a benign tumor, is a subject of great practical importance in the therapy of tumors. Tumor tissues undergo various changes in the same way that normal tissue does. They may become infected, necrotic, calcareous, etc. There is definite laboratory and clinical proof that benign tumors may change into malignant growths. For example, an adenoma may change into a carcinoma or a fibromyoma may become a sarcoma. There is also ample clinical proof that these changes are very rare.

If these changes were frequent the indication would be to remove all benign tumors in order to avoid the malignant change. This is sometimes the correct indication. More frequently benign tumors are removed because it is not possible to make a positive diagnosis, and to know that they are benign except by removal and microscopic examination.

Certain varieties of tumors show greater tendencies to become malignant than others. For example, a lipoma rarely changes to a malignant growth. An adenoma probably does more frequently.

The location of the tumor also influences the change in the malignancy of the growth. For example, a papilloma of the urinary bladder shows marked tendencies to become malignant. This tendency is so great that some observers believe that ultimately, if not removed, all such growths would become malignant.

Nevi, Warts, Etc.—Some warts are congenital, others appear during later years. During childhood, warts on the fingers arise without known cause and disappear as mysteriously. The warts and nevi that are congenital usually persist, and these, together with those

that appear later and persist, are of significance as possible precancerous lesions.

Keen, in 1904, reported 25 cases, of which 12 were from his own practice, of malignant change occurring in warts and moles. The fact that 12 cases of this kind occurred in the experience of one man, even though his experience was a large one, shows the importance of warts and nevi in their relation to cancer. In a number of these cases death resulted from recurrences or metastases after the operation.

The history of these cases is as follows: The wart or mole after existing as a benign tumor for a long period, that is, in some cases for forty years or more, shows signs of irritation or inflammation. At first the change is very slight, merely suggesting an inflammation about the wart or nevus. Later there may be ulceration and metastases in the skin, neighboring lymphatic glands, and distant organs.

In a number of cases, irritation or traumatism seemed to be the exciting cause. This irritation may be from clothing, combing of hair, occupation, and, in a number of cases, insufficient attempts at removal.

Usually the malignant change is to an epithelioma, sometimes to sarcoma.

Wilson and Kalteyer collected 50 cases of multiple sarcomata of the skin, and arranged them in three groups:

1. Multiple melanotic sarcomata . . .	26 per cent.
2. Multiple non-pigmented sarcomata . .	26 "
3. Multiple pigmented, hemorrhagic sarcomata	48 "

Of these cases of multiple sarcomata of the skin, in 69 per cent. the primary growth had its origin in a nevus or mole. Eves found in 33 cases of melanosarcoma, 26 cases began in pigmented moles.

These cases are sufficient to show that benign warts and nevi are sources of danger.

Keen advises the removal of warts and moles to avoid the possibility of malignant change. This obviously

would not apply to those cases in which there is a large number of moles scattered over the whole body. Any wart or nevus that is located in a place where it is exposed to constant or frequent irritation should certainly be removed. This would apply to all warts on the hands or feet, to those that may be irritated by clothing, such as collar, hat band, corset, etc., or by combing the hair or shaving, etc. Every wart or nevus should be removed at once if any sign of irritation develops.

After multiple malignant tumors have developed in the skin, little can be gained by any attempt to remove them.

Uterine Fibromata.—The question of uterine fibromata becoming sarcomata has long been a subject of interest to gynecologists. It is estimated that 20 per cent. of all women develop uterine fibromyomata, though they all do not give symptoms. It is known that uterine sarcomata are also frequent. Different laboratories estimate that from 2 to 8 per cent. of cases of supposed fibromyomata of the uterus that are removed, show elements of sarcomata. This indicates that fibromyomata and sarcomata are both frequent tumors of the uterus, but it does not demonstrate that the sarcoma is a later development of the fibroma. It must not be assumed, therefore, when sarcomatous tissue is found in a growth largely composed of fibrous tissue that it indicates that the benign fibromyoma has changed to a malignant sarcoma.

There are cases in which a fibromyoma of the uterus is involved by the extension to it of a sarcoma of the endometrium. Such a case, however, should not be considered as a change from a benign to a malignant growth.

There are reported in the literature well-authenticated cases of fibromyomata of the uterus undergoing sarcomatous transformation. These cases are very infrequent. They are so infrequent that some pathologists of wide experience state that they have never seen a case of fibro-

myoma of the uterus changing to a sarcoma. If a sarcoma is found it is probable that the sarcoma existed as such from the start.

A carcinoma has been described as developing in fibromyoma of the uterus, but this is probably less frequent than the sarcomatous change. Epithelial elements are described as being found in the interior of uterine fibromyomata, and in these a carcinoma may develop.

There are cases in which a carcinoma develops in the mucous membrane of a uterus containing a fibrous polyp as a result, it is believed by some observers, of the irritation caused by the polyp. Theoretically the contractions of the uterus in attempting to expel the polyp might produce irritation or repeated injuries that are believed to cause the development of the carcinoma. If the carcinoma develops in the polyp it would be an example of a benign tumor becoming malignant. If it developed in the uterine mucous membrane it would not be in the same class, but would illustrate the development of a malignant growth as a result of irritation by a benign growth.

Polypi of the Gastro-intestinal Tract.—An excellent example of a benign growth becoming malignant is seen in the benign polypi of the gastro-intestinal tract changing to carcinomata. According to Wolff, attention was first extensively directed to this change by Brissaud in 1885.

Polypi in the stomach and intestines are of common occurrence and are seen in young patients. They may be the outcome of embryonal defects in the mucous membrane or the result of inflammation or other cause. They are more common in the rectum and colon than higher in the gastro-intestinal canal, and are frequently multiple. These tumors may exist for a long period before any malignant change occurs.

The cause of the change is not clear. The tissue of which the polyp is composed is not normal. It is claimed by some that it is covered by modified epithelium, which is predisposed to a cancerous change.

There are two common factors, chronic irritation, and chronic inflammation, which are probably important influences in causing this change. The chronic irritation is partly from the intestinal contents and partly from the peristaltic action of the intestines. The chronic inflammation is partly from partial obstruction of the intestines, with the retention of feces, and partly from the chronic irritation.

Adenomata.—These tumors, though benign, have a definite histological relationship to carcinomata. As a rule they can be definitely distinguished from each other, but in some cases it is difficult or impossible to place a tumor absolutely in one or the other group. It is undoubtedly true that some cases of adenoma change and become malignant. Clinically this is certainly of frequent occurrence. The doubtful tumors, that is, the tumors that are difficult for the pathologist to place definitely in the benign or malignant class from the microscopic examinations, are usually of recent development.

In general, regarding the relationship of benign to malignant growths, it must be accepted that benign tumors show a greater disposition to become malignant than normal tissue.

It is true also in proportion to the total number of benign tumors that these changes are rare; that is, the type of a tumor usually remains the same and does not change.

Furthermore, these changes, when they occur, are often more apparent than real; that is, the malignant process starts in the tissues in the immediate vicinity of the benign growth, possibly due to irritation by the benign tumor which is involved only by extension.

The cause of the malignant change in a benign tumor is obscure. Usually the same agents that seem to have an influence in the development of the cancer elsewhere—that is, age, chronic inflammation, injury, irritation, etc.—are probably important factors in causing the malignant change.

CHAPTER III.

CONTAGIOUSNESS OF CANCER.

Among the ancient writers, cancer was considered to be contagious; that is, that the disease could be transmitted from man to man, also from man to animal, and from animal to man. It was believed that the contagion was transmitted through the air by the cancer vapors, or by the cancer juice, or by the cancer cells, or by cancer parasites.

Wolff, from the literature of several centuries ago, gives examples of cases that were supposed to have developed from infection transmitted in these various ways. For example, the vapor from an ulcerating carcinoma of the breast was claimed to have caused cancer. A woman was reported to have developed a cancer of the neck directly after drinking water that had been contaminated by "cancer juice" from dressings from a carcinoma. A case is given of a girl who developed a cancer twenty years after drinking water containing "cancer juice." To illustrate the transmission of cancer from man to animal, there is quoted the case of a dog licking the cancerous lip of his master and later developing cancer. Also of a dog developing a cancer of the stomach after eating cancerous tissue.

In more recent literature, to illustrate the contagiousness of cancer through the medium of cancer cells, cases of "cancer à deux," that is, cases of cancer occurring in two people living in close relationship as, for example, husband and wife, are quoted. A number of cases are reported of cancer of the penis and of the uterus occurring in husbands and wives.

These cases well illustrate the opinions that have held during different periods of the contagiousness of cancer. First, that it might be transmitted through the air, then that it might be transmitted through the air only after the growth had become ulcerated, later that contact, especially with mucous membrane, was necessary, and finally, that repeated contact and probable introduction of cancer cells into microscopic injuries, was necessary in order to transmit cancer.

The evidence of the contagiousness of cancer that is contained in such cases in the literature is further supported by two facts in regard to cancer that are universally known. Certain forms of cancer in some animals can beyond question be transmitted from one animal to another of the same species. This is the case with certain cancers in mice. If a mouse cancer can be transmitted from one mouse to another it is a strong argument that some cancers, and of course there are many varieties of cancer, can be transmitted from one human to another. The second fact is one concerning which there is no doubt; in fact, one that is included in most definitions of cancer. It is that a cancer can be transmitted from one place to many different parts of the same individual. This can happen not only through metastases in the natural course of the growth, but also by implantation in the surgical wound.

It is not strange, with the evidence of the cases reported, supported by other known facts in regard to cancer, that its possible contagiousness is constantly before the medical profession, and always in the minds of the laity.

As a matter of fact, however, the cases reported are either unreliable or the condition can better be explained in other ways, and practically cancer is not considered contagious.

The possibility of contagion through the atmosphere by cancer vapors is too far removed from the ideas of modern medicine to be further considered.

Dogs have been fed on cancerous tissue without their

developing cancer. This would indicate that cancer cannot experimentally be transmitted from man to dog, either through contact of mucous membrane with cancer or by the ingestion of cancer juices.

It is not difficult to disprove the evidence that cancer is contagious, that is given when cancer develops in one member of a family shortly after a similar one in another member. This is true even when it concerns a cancer of the penis and a cancer of the cervix uteri or some part of the vaginal tract. The evidence of the contagiousness of cancer furnished by cases of this kind is of limited value.

Carcinoma of the uterus is a common disease; there are thousands of cases every year. Even though carcinoma of the penis is relatively rare, it must be accepted that by chance occasionally a carcinoma of the penis and of the uterus should occur in a husband and wife. This combination must be infrequent, because such cases are of such peculiar interest that they would be found more often in the general literature if of common occurrence.

The more practical and stronger evidence against the contagiousness of cancer is that cases that have apparently developed as the result of contagion are not seen by men of wide experience. Cancer is a very common disease, and there are an enormous number of cases in the ulcerative stage, the stage in which the greatest contagiousness would be expected, which are being cared for by members of the family of the patient, that is, by people not specially trained to avoid infection. If cancer were contagious, evidence of it would be found in some of the numerous families.

Further practical evidence that cancer is not contagious is seen in surgical work. Throughout the world in every civilized country, surgeons are daily operating upon thousands of cases of cancer. Surgeons, through small cuts and needle pricks, received during operation become infected by syphilis, pyogenic organisms, etc., but they do not become infected with cancer. If cancer were

contagious, there would surely be examples in this vast amount of possible material.

It can be assumed, therefore, that in the sense of being transmitted from one person to another, under ordinary conditions, cancer is not contagious.

Recurrences.—By this term is meant the reappearance of the disease after its removal in the immediate vicinity of the original growth. Ancient writers believed that a recurrence was, as its name implies, a return of the cancer after it had been completely removed. The present belief, and undoubtedly the correct one, is that the original malignant growth was not entirely removed. In other words, the recurrence is a definite and direct continuation of the original growth, of which at least a microscopic part was not removed.

The recurrence is most frequently in the scar or in the tissue that was nearest to the original growth. At other times it is near the scar but separated from it by an interval of normal tissue.

There are three ways by which cancer cells are left in the tissues and recurrences result:

1. Cancer cells may exist previous to the operation, outside the area of tissue removed at the operation.

2. Cancer cells during an examination or the operation may be mechanically forced into the area outside of the tissue originally involved.

3. By implantation, that is, cancer cells from the primary growth may be implanted on the surface of the operative wound and be the starting of a new growth.

The knowledge and consideration of these three reasons why recurrences of cancer take place are of the greatest practical value and modify the modern treatment and operative technique of cancer.

1. In the description of metastases, and also in the chapter on Carcinoma of the Breast, the presence of cancer cells in the lymphatic vessels, and also to a less extent in the veins and tissues, has been described. All modern operations for cancer are based on the knowledge

that to remove all of it, not only all the tissue that macroscopically is diseased must be removed, but also a wide area of tissue that is apparently normal, otherwise tissue containing the microscopic cancer cells will be left and a recurrence will occur. In doing this, particular attention is given to the tissues that are known to contain cancer cells most frequently. The result of this is that in the modern operations for cancer the organ or parts in which it is located is removed as widely as the anatomical relations will allow. This is well illustrated in the present operation for cancer of the breast. Not only is the entire breast removed with the cancer but also a wide area of skin and a wider area of the deep fascia, the pectoral muscles and the axillary lymphatic glands. Each step in the development of the operation has made it more extensive and also increased the percentage of permanent cures.

2. The mechanical displacement of cancer cells by manipulation is an undoubted cause of some recurrences following operation, and is a possibility that should be more generally appreciated both by the physician and the patient. There is no doubt that through ignorance the spread of cancer cells is favored by improper handling of the growth.

Under proper circumstances, rubbing or massage of a swelling such as may result from injury or inflammation is the proper treatment. This knowledge is frequently used by the patient without consulting a physician. When massage is used on a swelling which may be a cancer, as, for example, a swelling in the breast, it is associated with great danger and doubtless the favorable outcome of many operations for cancer has been made impossible by this improper treatment.

The manipulation of a malignant growth by a physician in an examination is associated with the same risk of displacing cancer cells as any other manipulation. For this reason, any examination of a possible cancer should be associated with the greatest gentleness, and repeated

examinations, unless necessary, should be avoided. The seriousness of many operations for cancer and the desire of both patient and surgeon for consultation may require more than a single examination, but the danger should be remembered and the smallest amount of manipulation possible should be used.

To avoid the mechanical risk of scattering cancer cells, cancerous tissue should not unnecessarily be cut into either during or before an operation. There are some uncertain and doubtful cases that cannot be diagnosed with sufficient certainty to warrant an extensive operation without a microscopic examination of a piece of the tissue. The common custom, therefore, of removing such pieces of tissue for immediate microscopic examination of a frozen section of it is necessary in some cases. The danger of scattering cancer cells can be lessened, in some cases, as in carcinoma of the cervix uteri, by removing the piece of tissue for examination with the cautery. In other cases, as in some tumors of the breast, the danger can be lessened, if not entirely avoided, by removing the entire tumor with some additional tissue apparently normal about it instead of incising into the tumor itself. Some reliable observers state that the statistics of operations for cancer of the breast that have not had a preliminary excision of a piece of it for microscopic examination are more favorable than those that have had a piece excised.

3. **Implantation Recurrences.**—While cancer cannot be transferred from one person to another, it can be transferred from one to another part of the same individual. One example of this is the formation of metastases. Another less frequent example of the transference of cancer from one part of the body to another is that which occurs as the result of direct contact of the cancer or the cancer cells with a wound. The danger of such infection is one reason for not allowing a sloughing cancer or its cut surface to come in contact with the wound of the operation. The possibility of transplanting cancer

in this way was long questioned, but the cases seen and reported by different observers are too common and definite to leave any doubt in regard to it. The most convincing cases are those in which a cancer develops in the scar of an abdominal wound within a few months after the removal of a malignant growth from the abdomen.

The anatomical relations of the scar to the original growth excludes the possibility that the growth in the scar is either a local recurrence or a metastasis. It can naturally be explained only as an implantation. There can be little doubt that such a growth in the abdominal wound is the direct result of cancer cells being deposited on the wound surface at the time of the operation.

Another example of the recurrence occurring in a wound about which there can be no question is the growth which occurs along the wound made by a trocar in tapping a malignant papilloma of the ovary or the abdomen in a similar case in which the peritoneum has been secondarily involved. The conditions are all extremely favorable for the formation of such a secondary growth. The cancer cells or the pieces of cancerous tissues are sterile, and are deposited along the course of the wound that is also sterile, and which is at once closed so that no outside influence may interfere with the growth of the malignant cells in their new location. There are a number of cases of this kind reported in the literature. Cullen reports such a case. A papillary cyst of the ovary was tapped. Several weeks later an exploratory laparotomy was performed, and in the abdominal wall beneath the skin and along the track of the trocar were found multiple growths, which had the histological characteristics of the ovarian growth.

Implantations in the vagina during operations for carcinoma of the uterus may occur in two places. In performing a vaginal hysterectomy for carcinoma of the uterus, it is necessary in the cases with narrow vaginæ to make an incision on one or both sides of the vulva to widen the orifice. A number of cases have been reported

in which carcinoma has developed in the incisions. It is obvious that such cases can only be the result of implantation of cancer cells during the operation, as neither local recurrences nor metastases would be likely to occur in such places.

The second place in which cancer cells are undoubtedly implanted during the operation for cancer of the uterus is in the wound in the top of the vagina. With many cases of carcinoma of the cervix uteri which are considered operable, it is technically impossible to keep the cancer surface always away from the cut edge of the vaginal wound. To avoid the implantation that might therefore otherwise occur, it is usual in these cases for the surgeon to destroy as much as possible of the cancer with the cautery before any incision is made. It is best also to make the incision through the vaginal wall with the cautery. It is well known that the recurrence following an operation for carcinoma of the uterus is most frequently in the vaginal scar. It is not possible to state that this is due to implantation of cancer cells at the time of the operation with the same certainty as when it occurs in the lower vulva incisions. The local recurrence may be due to local extension of cancer tissue that existed previous to the operation and beyond the parts removed. It is probable, however, when the recurrence is in the top of the vagina and not in the bases of the broad ligament at the sides, that it is due to the implantation of cancer cells at the time of the operation. Certainly it is of the greatest importance that the possibility of such implantation is considered in all operations for cancer of the uterus.

Time of Recurrence.—It is probable if cancer cells remain in the tissues after an operation, that they continue to proliferate; but as the term "recurrence," as it is commonly and loosely used, really means reappearance, the time of recurrence really means the time at which the recurrence can be demonstrated. It is becoming more and more evident that it is not possible to give

the late limits at which a recurrence may occur. The general statement that the longer the period that has elapsed since the operation the less likely is the growth to recur, is more nearly true than any other that can be made. Formerly three years was arbitrarily taken as the time which must elapse before a cancer case could be considered "cured." It is necessary to have some fixed limit for statistical purposes, and as it was found that there were numerous recurrences after the three-year period, the time was lengthened to five years. It is now generally accepted in all countries that five years must have passed since an operation for cancer before the case can be reported as "cured," and that at that time the case can be so considered, though later recurrences are known to occur.

As a rule, recurrences take place early, but statistics in regard to the time are indefinite and are influenced by the location and by the extent of the primary growth. If the primary tumor was located in an organ that is easily accessible to examination, a recurrence as well as the primary tumor would be recognized early. In a more inaccessible organ a recurrence could not be demonstrated until it had reached a more advanced stage. The period at which a recurrence takes place also depends on the extent and malignancy of the primary tumor. A series of advanced cases will give an early list of recurrences.

Late Recurrences.—The usual rule that if any cancer cells remain in the tissues that they begin at once to proliferate and grow is by no means absolute. Beyond doubt, as is discussed in the section on spontaneous cures, not all cancer cells remaining in the tissues continue to grow. There is definite clinical evidence that, though diseased tissue was present and not removed at the time of the operation for cancer, yet the case remains permanently cured. In other cases the growth of the cancer cells are held in check for a time. If, for example, following an operation for cancer of the breast, a small nodule appears only at the end of three or four years, it must be

accepted that it has not been growing during this entire period or else it would have been palpable at an earlier time.

By late recurrences are usually meant those that occur five or more years after the operation for the removal of the primary tumor. There are numerous cases in the literature of recurrences in the immediate vicinity of the wound at the end of ten, fifteen and twenty years. There are two possibilities in regard to these late recurrences: By some, they are considered to be not recurrences but second primary growths which developed in the scar or in the neighboring tissue and had no direct relationship with the original tumor. The similarity of the histological structure of the primary growth and the late recurrence would be against this explanation for all cases.

Another explanation is that the cancer cells, though remaining alive, become encysted or walled in by the tissues in the same way that any foreign body may be. After a period of years, as a result of traumatism, of disturbed metabolism or of causes with which we are not familiar, these cells become freed, begin to grow and produce the late recurrence.

The conditions that control all recurrences are closely related to the specific cause or causes of cancer. Until more is known about these causes of cancer in general, it is probable that the real reasons for the late recurrences will remain concealed.

It must be remembered that these late recurrences are rare and constitute a very small percentage of the cases. It is probable that the chances of a recurrence after the period of five years are less than if the original tumor had not developed and the organ in which it was situated had not been removed. There is always a risk that carcinoma may develop in an organ. The woman, for example, whose uterus or breast has been removed for carcinoma probably runs less risk of a recurrence after a period of five years than a woman whose breast or uterus has not been removed runs of developing a primary tumor in one of these organs.

METASTASES.

A metastasis is the spread of a disease from one part of the body to other organs or structures. For example, there may be an original or primary lesion in the breast, and from this primary lesion in the breast other organs, such as the liver or spleen, may be involved by secondary growths. These secondary growths are spoken of as metastases. The most frequent use of the word is in regard to malignant disease. While the word metastases is used most frequently in regard to malignant conditions, it is not its only use. In pyemia, for example, the original lesion or focus may be in the uterus, and from that original lesion secondary abscesses may develop in other organs, such as the liver or parotid gland. These secondary abscesses may be and frequently are spoken of as "metastatic abscesses."

Care must be taken not to confuse the term metastasis with recurrence. A metastasis is the appearance of the disease in a distant part, and in many cases is the natural way by which the growth progresses. A recurrence is a return or, better, the reappearance of a malignant process in the immediate vicinity of the primary growth, and the term carries with it the implication that an attempt was made to remove the original growth. While the term recurrence is in frequent usage and will remain so, it is not strictly correct. Strictly, the word implies that the original disease was removed and that later it returned or recurred. As a matter of fact it was not entirely removed. If it were entirely removed it would not come back, and the fact that there is a recurrence proves that a part of the disease, possibly microscopic in size, was not removed. A metastases has no reference to an operation or other therapeutic measure, it is a part of the natural progress of the disease.

Ancient writers recognized that malignant growths were followed or accompanied by metastases in distant organs, but it long remained obscure how they occurred.

At one time it was believed that the metastatic growths as well as the primary lesion were the result of a general diathesis, and that there existed in the body certain "humors" which circulated in the blood and caused the cancerous growths. Later it was recognized that the growths in various parts of the body came from a single primary tumor and it was then believed that the primary tumor produced the "humor" in the form of a "cancer juice" which by osmosis or in some other way gained access to the blood, circulated to various parts of the body and produced the secondary growths.

It is now known that cancer cells from the primary tumor are the cause of the metastatic growths. These cells are transferred from the primary tumor to distant parts chiefly in three ways:

1. Lymphatic system.
2. Venous system.
3. Arterial system.

In general the importance of the systems in spreading cancer throughout the body is in the order named. It is generally believed that carcinomata spread mostly through the lymphatics and sarcomata through the bloodvessels. This idea is doubted by others who claim that the sarcoma cells enter the lymphatic system with the same frequency as the carcinoma cells, but on account of their size and shape they are not filtered out by the lymphatic glands and so pass on to the vascular system; that is, the sarcoma cells reach the vascular system more frequently than the carcinoma cells, but they do so indirectly through the lymphatic system.

The Lymphatic System.—Cancer cells from the primary growth may escape into the lymphatic vessels. These cells may become lodged at any point in the lymphatic vessel, begin to proliferate and produce a secondary growth in the vicinity of the primary tumor. The lymphatic vessel for a considerable distance may be filled with cancer cells, partly from the primary growth and partly by the proliferation, forming a definite chain

of carcinomatous nodules, the so-called lymphangitis carcinomatosa.

Instead of being stopped in the lymphatic vessel, the cancer cells may be carried by the lymph stream to the lymphatic gland. The lymphatic gland acts as a filter, and for a time at least, the further spread of the disease in this direction is checked. In the lymphatic gland, the cancer cells may be destroyed or they may proliferate and produce a secondary growth or metastasis in the gland.

The metastases in the neighboring lymphatic glands are usually the first secondary growths that are formed. Histologically the secondary growth in the gland corresponds to the primary tumor. The gland becomes enlarged and hard and gradually takes on the same characteristics as if it were a primary tumor. First one and later a number of glands of a set or chain are involved.

The regularity with which the lymph nodes are involved and enlarged, at some stage of carcinoma of an organ, makes the enlargement of these glands a valuable diagnostic sign. For each organ there is a definite set of glands in which a metastatic growth may first be expected, and the presence or absence of the enlargement of such glands is one of the best indications of the extent and duration of the growth. If there is no enlargement of the glands, it is probable that the growth is of short duration, of limited extent, and more favorable for operation. The enlargement of the glands does not necessarily indicate the opposite, because it may be due to other causes than a cancerous involvement on to an early metastasis.

In some cases, the first chain of lymphatic glands is not involved, but the second is. For example, from a carcinoma of the hand the glands of the axilla may be involved before those at the elbow. It is possible in such a case that the cancer cells pass through the first set of glands and are checked by the second. The more probable explanation is that the lymphatic vessels, sometimes in an atypical manner, carry the cancer cells around the first set of glands directly to the second chain.

The lymphatic glands can check the spread of a malignant disease only for a time. Cancer cells from a secondary growth can gain access to the distal lymphatic vessels in the same manner as from the primary tumor. After the involvement of one or more sets or chains of lymphatic glands, the last barrier is passed and the cancer cells enter the general vascular system through the thoracic or other lymphatic channel. After the vascular system has been entered the cancer cells can be carried to any part of the body.

Venous System.—Cancer cells may enter the venous system indirectly by passing first into the lymphatic system, as has been described, or may enter it directly by the involvement of the wall of the vein itself. As the cancer grows the wall of the vein may be invaded in the same way as other structures, and when the intima is reached and eroded, the cancer is in direct contact with the blood current. In this way cancer cells may be spread throughout the body through the vascular system. By the continued growth of the cancer, the lumen of the vein may be filled with the cancer cells to such an extent that it is entirely obstructed.

As a rule the metastases from the direct involvement of the vein come at a later stage than those through the lymphatic system. They may, however, occur earlier. Usually the smaller veins are the only ones involved, but in some cases the largest veins are directly affected. For example, Kantorowicz describes a case of carcinoma of the breast in which the subclavian vein was directly involved. It has been noticed that when the large veins are directly involved, the metastases are very numerous even in organs not frequently involved, and the course of the disease from then on is a rapid one.

Some cases have been reported in which the veins have been involved without metastases. These cases are infrequent and probably occur shortly before death, and there has not been sufficient time for metastases to be formed after the growth has invaded the vein.

Arterial System.—Metastases through the arteries are less frequent than following invasion of the veins. The walls of the arteries are thicker and more resistant to the invasion of the growth. When the arteries are invaded, the cancer cells are carried toward the periphery and would be caught in the capillaries. There are cases on record in which large arteries, even the aorta, have been invaded in the progress of a malignant growth and a fatal hemorrhage the result. These cases are rare.

Retrograde Metastases.—Metastases sometimes occur in locations that are explained by accepting the theory that they have formed against the flow in the lymph or venous system. They are called retrograde metastases. It has been demonstrated, clinically and experimentally, that there is a reversal of the current in the lymphatic vessels or in the veins, and that it flows in a direction opposite to the normal. It is conceivable, that in the abnormal conditions produced by a malignant growth, that this may sometimes happen in small vessels in the immediate vicinity of the growth. It is doubtful if it does to any great extent, particularly at a distance from the growth. The more usually accepted theory is that the malignant tumor grows rapidly along the lymphatic vessels or the veins. The lumen of the vessel may be occluded by the proliferation of the cancer cells, so that the natural flow in the vessels is entirely stopped. Under these conditions the cancer may grow more rapidly along or in the vessels than in the surrounding tissue, and at some point a lymphatic vessel or vein is reached in which the current runs normally in the opposite direction, and in which the cancer cells are carried to the parts supplied by it.

Peritoneal Metastases.—When cancer cells reach the peritoneal cavity either from a cancer of one of the abdominal viscera extending through the peritoneal layer, or from any organ of the body through the lymphatic system, metastases may be formed in ways different from those described.

Cancer cells or pieces of malignant tissue may be de-

tached from the primary growth in the peritoneal cavity and be carried by gravity from the upper to the lower part of the abdominal cavity and, becoming engrafted, form metastases there. Metastases on the anterior wall of the rectum occur from a primary carcinoma of the stomach and is a sign that the primary growth has penetrated the peritoneal layer and that the case is inoperable. Metastases in the ovaries are also seen from a carcinoma of the stomach. In both these instances the cancer cells are believed to have been carried by gravity from the stomach to the pelvis.

The movement of the abdominal viscera is responsible for some peritoneal metastases. In cases of ovarian papillomata the entire peritoneal cavity may be covered by small metastases. It is difficult to explain these numerous metastases on the peritoneum in any way except by the spread of cancer cells, by the movements of the abdominal viscera, or by the natural movement of the peritoneal fluid in the abdominal cavity. Some of the metastases that appear to be in the peritoneal cavity are really beneath the peritoneum. These must have originated in other ways, that is, through the lymphatic or vascular systems.

In the thoracic cavity metastases may occur in the same way as in the peritoneal cavity.

EXTENSION BY CONTACT OR IMPLANTATION.

These are sometimes spoken of as implantation metastases. There are numerous cases in the literature that confirm the belief that if a cancer remains constantly in contact with tissue, cancer cells will be implanted and a cancerous growth formed in it similar, histologically, to the primary growth. That this secondary growth is not due to the irritation is proved by the similar histological structure of the two growths.

Implantation on Serous Membranes.—After a malignant papilloma of the ovary has perforated the cyst wall, the

peritoneum is soon covered by small papillomatous outgrowths similar, histologically, to the primary tumor. The majority of these small papillomata are the result of papillomatous cells being carried by the lymph currents and the movement of the abdominal viscera throughout the peritoneal cavity. Undoubtedly some of these secondary growths result through adhesions of the primary growth with surrounding structures and the direct extension of the malignant process through these organized adhesions. Neither of these methods correctly illustrate contact infection. There is no doubt, however, that direct contact infection does occur in the abdominal cavity. While there may be some question regarding the possibility of contact infection between a septic, sloughing carcinoma and normal mucous membrane as, for example, between a carcinoma of the cervix uteri and the vagina, there can be no doubt about it, in regard to a papilloma of the ovary in the peritoneal cavity. In this case the malignant growth is not septic and the peritoneum and omentum readily become attached to a growth or other abnormal mass in the abdominal cavity. If it is accepted that free cancer cells in the peritoneal cavity can become attached to the peritoneum and form secondary growths, it is easy to believe that cancer cells that are still a part of the primary growth and are still nourished by it may form a secondary growth by contact.

There can be little or no doubt that implantation of cancer by contact with serous membrane takes place not only in the peritoneal but also in the thoracic cavity.

Implantation on Mucous Membrane.—The most frequent example that is seen of this occurs in the vagina from a carcinoma of the cervix uteri. It is doubtful if cancer cells can be implanted and grow on normal mucous membrane. It is more probable that the hard, everted edges of the malignant growth in the cervix uteri, by frequent movements, first irritates and erodes the vaginal mucous membrane and then the cancer cells become implanted on the wound surface.

Against such a method of implantation of cancer, it is urged that a carcinoma of the cervix uteri is always infected and that the implantation of cancer cells in the presence of infection is not possible. There can be no doubt that the presence of this infection is unfavorable to the formation of a contact growth. If it is remembered that the primary growth is constantly in contact with the erosion in the vaginal mucous membrane, it must be accepted that the probabilities are in favor of cancer cells being so implanted in some cases that they will continue to grow.

A further argument against these secondary growths in the vagina being true contact cancers is that they can be explained in another way, which to some observers seems more rational. These observers claim that these growths are retrograde metastases; that is, that they are metastases formed by cancer cells being carried in lymphatic vessels or veins in which the direction of the flow has been reversed. In support of this view are mentioned those cases in which there are beneath the vaginal mucous membrane malignant growths secondary to a carcinoma of the cervix. This is frequently seen in cases of chorio-epithelioma of the uterus. These cases of submucous growths cannot, on account of their locations, be contact growths, but if they were not seen until a later stage when they had ulcerated, they would have all the appearance of such growths and might erroneously be so considered.

It is probable that some of the cases of secondary growths in the vagina are due to retrograde metastases and that some are due to contact implantation.

There is another method of implantation on mucous membrane that is described, and about which there is much more doubt. There are cases reported in which it is supposed that a secondary cancer of the stomach is produced by swallowing pieces of cancer tissue or cancer cells from a cancer of the tongue or cheek. In the same way a secondary growth of the intestine is believed to result from a primary tumor higher in the gastro-intestinal

tract. Cases are reported of carcinomata of the lungs resulting from the implantation of cancer cells or tissue from a similar growth in the larynx or trachea.

It is exceedingly doubtful whether cases of this kind ever occur. In the gastro-intestinal tract, it is doubtful if minute pieces of cancerous tissue could withstand the action of the digestive juices. Differing from the cases of contact cancer of the vagina, in these cases the cancer is not in continuous contact with the eroded or diseased mucous membrane. It would be much more rational to explain these cases as multiple primary tumors. Carcinoma of the tongue and of the stomach are frequent diseases, and chance would bring them together in the same individual as frequently as implantation tumors of this kind are supposed to exist.

It is difficult to believe that cancer cells from a growth in the larynx could obtain lodgment and grow in the mucous membrane of the smaller bronchi. It is more probable that any piece of tissue would be treated as a foreign body and be expelled or encysted.

Cases of contact cancer are also reported between the upper and lower lips, between the tongue and cheek, and between the two sides of the vulva. In each of these instances, the primary cancer is in constant contact with the opposite tissue, and it is probable that true contact cancers are seen in these places.

Implantation on the Skin.—It must not be supposed that a cancer can be engrafted on the normal skin. As with the mucous membrane, the skin must be eroded and ulcerated before the cancer cells can be implanted. The most frequent cases of this kind are seen about the breast. Either in a heavy pendulous breast, the ulcerated carcinoma is in contact with the skin of the chest wall, or the location of the growth brings it in contact with the upper arm. First, a simple ulceration is formed and on this the cancer cells become implanted.

Fate of Cancer Cells Entering the Circulation.—As has been described, cancer cells become separated from the

primary tumor, enter the lymphatic, venous and arterial systems and are carried to various parts of the body, forming the secondary growths or metastases. It is not believed that all the cancer cells that leave the primary tumor in this way ultimately form the metastases, but that many of them are destroyed.

In the lymphatic glands, beyond doubt many cancer cells are destroyed. It is probable that a growth while still small and in an early stage may give off cells and that these are destroyed in the lymphatic glands. These glands probably act toward cancer cells as they do toward other detached body cells. It is only after the lymphatic glands have been overwhelmed, after they have been given more work than they can accomplish, that the cancer cells obtain a lodgment and form a metastasis. Even then the action of the lymphatic glands in destroying cancer cells goes on, as is shown by the spontaneous cure of metastases in such glands.

In the veins and arteries, cancer cells are carried to the various parts of the body. In the arterial system the blood is carried to the minute capillaries into which the arteries divide. Any foreign bodies in the arterial system are ordinarily lodged evenly in the capillaries throughout the body, that is, the muscles, bones, viscera, etc., all have deposited in them approximately the same amount of the foreign substances. This is not the rule in regard to the formation of metastases in malignant diseases. Certain organs, such as the liver and lungs frequently show metastatic deposits; other structures, such as the muscles, rarely show these secondary growths. It is assumed, therefore, that at some point the cancer cells that are carried to the muscles are destroyed to a greater extent than those that are carried to the liver and lungs.

There is no way to know how many cancer cells enter the blood from the primary and numerous secondary growths. It is not conceivable that the number is as small as the number of metastases that are found in

malignant conditions. It is probable, judging by the knowledge of other conditions, that the entrance of cancer cells into the circulation is a frequent and not an unusual occurrence. If each cancer cell that entered the blood found ultimate lodgment and became a metastatic growth, the number of such growths would probably soon become very large, much larger than are usually found.

It is not possible to tell exactly where the cancer cells that enter the blood and fail to produce a metastatic growth are destroyed. It may be in the blood; it may be in the tissues after the cells have become lodged. It is most probable that it is in the tissues, and not in the circulating blood.

CACHEXIA.

Cachexia is the late constitutional manifestations of the malignant process. The general clinical picture is quite characteristic of cancer, and the term cachexia is generally applied to the condition that results from the cancerous growth; there is, however, nothing that is really distinctive about cancerous cachexia. Any of the known changes and a similar picture may be produced by other diseases and the term cachexia might be, and in fact is, sometimes applied to the general condition seen in the terminal stage of various chronic exhausting diseases. The term is, however, more frequently applied to constitutional conditions of a patient in the late stage of a malignant growth.

The *time* at which cachexia appears varies in different cases, and depends both on the type of the growth and the organ in which it is situated. In general, there is less cachexia in sarcomata than in carcinomata, though there are marked exceptions. The cachexia in the mildly malignant epithelioma of the face comes much later and is less marked than in the rapidly growing carcinoma of the breast. The cachexia of a carcinoma of the cervix uteri which sloughs early and may be the source of a secondary infection, appears earlier and is more marked than in a

growth that does not ulcerate until later, if at all. A carcinoma of an organ necessary for nutrition and life, such as the stomach, liver, etc., causes cachexia earlier than a similar growth in a less important organ, such as the uterus or breast.

Cause.—The cause of the cachexia cannot be assigned to a single influence. By the ancient writers the cachexia of a malignant growth was looked upon as a separate disease and not as a result of the cancer. Later, when "cancer juice" was looked upon as the active agent of cancer and as the cause of all local and general manifestations of the malignant process, its absorption in the blood and general system was considered the cause of the cachexia. Still later this idea of the absorption of the "cancer juice" was modified, and the breaking down and absorption of the cancerous tissue of the growth itself was believed to produce the cachexia. At present many writers believe the absorption of the products of the cancer cells that have entered the blood as such is the principal cause of the cachexia.

In general, all of these different theories agreed that the cause of the cachexia is the absorption of products of one kind or another from the growth which were injurious to the various body functions.

With our present beliefs, part of which are based on theoretical knowledge and part on clinical experience, the causes of the cachexia can practically be arranged under two headings: (1) Absorption of decomposition products, toxines, etc., from the primary tumor and its metastases, and (2) interference with the functions of the various organs.

Probably the most important absorption products are from the destruction of cancer cells after they have entered the blood or lymphatic vessels. It is probable that the absorption of the products resulting from the destruction of cancer cells begins early. It has been repeatedly demonstrated that the lymphatic glands near a malignant tumor show early signs of special activity even when

there is no metastatic growth in them. This would indicate that cancer cells or other tumor products enter the lymphatic glands even at this early stage. A careful examination will detect the results of this absorption before general cachexia has developed. For instance, there may be changes in the blood or an irregular fever.

A second form of absorption from a malignant tumor occurs when it breaks down and becomes secondarily infected. The absorption of these septic products has the same effect as a similar process would under other conditions.

It is quite possible that there are also other absorption processes going on from the malignant growth of which nothing is now known and which are etiological factors in cachexia.

Interference with the functions of organs may be caused in two ways: There may be first, the mechanical interference due to the presence of the malignant growth. A cancer of the esophagus, stomach, or intestine may mechanically interfere with the function of one of these organs, which would interfere with the nutrition of the patient and in this indirect manner add to the rapidity and extent of the cachexia. Other cancers will add mechanically to the cachexia, depending on the organ in which they are situated.

The second way in which the functions of organs are interfered with by a malignant growth, is through the absorption of toxic products. That is, the absorption of toxins may interfere with the function of such organs as the stomach, liver, etc., and in this indirect manner may increase the cachexia.

The *blood* changes in malignant tumors is, according to Naegeli, due to four causes:

1. The action of the toxins on the blood-forming organs.
2. Secondary infections.
3. Destruction of blood-forming organs by the primary growth or its metastases.

The extent of the changes in the different elements

of the blood depends on the type, stage, location, and extent of the growth.

The red blood cells are usually reduced in number if the case is at all advanced. In most cases the reduction in the number of red blood cells will be present before other symptoms of cachexia will appear. The lowest count in Cabot's series of cases was 1,457,000; other observers report numerous cases below 1,000,000.

In some cases there may be no diminution in the red blood cell count, even though the case is well advanced, and in still other cases the red cell count may be actually considerably increased. These conditions are due to a concentration of the blood and not due to an increase in the actual number of red blood cells. The concentration of the blood and increase in the red blood cell count is seen in malignant tumors that interfere with taking and absorbing fluids, such, for example, as carcinoma of the esophagus or stomach. In Cabot's series of 129 cases of gastric cancer, there were over 6,000,000 red cells in 4 cases and between 5,000,000 and 6,000,000 in 23 cases.

As a rule, the hemoglobin percentage is low. In 87 cases of malignant tumors in the series of Cabot, the hemoglobin ranged from 20 to 100 per cent., with an average of 58 per cent. The percentage of hemoglobin may be low even with a normal red blood count.

Morphologically there are marked changes in the red blood cells. Their size may be decreased. In advanced cases, and in some early cases, nucleated red blood cells are usually found. Usually the nucleated red blood cells are of normal size but they may be increased. The shape of the red blood cells may also be changed.

The white blood cell count is usually moderately increased. In 91 cases of malignant disease Cunliffe found an average total white count of 14,864. The highest average white counts found by Cunliffe were in the cancers of the cervix uteri (22,800) and of the stomach (17,280). The high count in these cases illustrates the influence of bleeding and infection in causing a leuko-

cytosis in carcinomata. The nature of these cases is such that both bleeding and infection were present. In one case, reported by Cunliffe, of a carcinoma of the cervix uteri with repeated hemorrhages and ulcerations into the bladder and rectum the total count was 59,200. Such a high count is, of course, very exceptional. In a few cases the white blood count is decreased. Cabot speaks of the decrease in some cases of carcinoma of the esophagus due to starvation. Cunliffe found a count of only 32,000 white cells (the smallest number in his series) in a case with mildly malignant growths of the peritoneum.

The causes of leukocytosis in malignant tumors are found in the complications rather than in the growth itself. These complications are hemorrhage, ulceration and infection, metastases, and rapid growth. The leukocytosis may disappear with the removal of the growth by operation and return if there is a recurrence. Some observers believe that an increasing leukocyte count indicates a return of the disease. A recurrence large enough to cause a leukocytosis could probably be recognized in most situations by other means, and the diagnostic help of such an examination would not be great.

Symptoms.—The symptoms of the cachexia are gradual but progressive. The rapidity with which they develop is subject to wide variations. The color of the patient is described as a straw pallor, and is not unlike that of secondary anemia. The change in color is due mostly to the diminution of the hemoglobin in the red blood cells.

The *emaciation* is a late symptom, but is usually present before the termination of the disease. There are, however, exceptions to this rule. The emaciation is due to disturbances of the gastro-intestinal tract, with the resulting loss of appetite, nausea, vomiting, etc.

Pain may be local in the primary growth or in the metastases or reflected from them. There also may be pains suggesting rheumatism in different parts of the body from the absorption of toxic substances. There are also exceptions in regard to the presence of pain.

Occasionally a patient with a cancer may have neither local nor general pain during any part of its course. Frequently the secondary infection of the ulcerated growth is the cause of the greatest amount of pain. Much can be done for the relief of pain in such a case by keeping the wound clean.

Fever is usually considered to be absent in cases of cancer if there is no ulceration or secondary infection. If there is an increase in the temperature and ulceration and infection of the growth are present they are sufficient to explain it, and are probably the real cause.

In the absence of ulceration and infection it is more difficult to explain the slight increase in the temperature that is present in some cancer cases. The most probable explanation is the absorption of decomposition products or toxins from the tumor or its metastases. It is believed by some observers that a temperature is more often present and more marked if the primary growth or its metastases are in the parotid gland, the liver or the blood-forming organs, also if the cancer is of the acute, rapidly growing type, such, for example, as is sometimes seen in the breast during pregnancy.

A different type of fever is seen in some cases, especially in those cases which are greatly emaciated and have been largely without food for some days, shortly before the final termination of the case.

Coma is the terminal condition in occasional cases. This was first specially described by Jaksch.

LITERATURE.

Cunliffe. Medical Chronicle, September, 1903.
Jaksch. Wien. klin. Woch., 1883, Band xxxiii, S. 473 and 521.
Wolff. Die Lehre von der Krebs Krankheit.

CHAPTER IV.

SPONTANEOUS CURE OF CANCER.

Formerly it was believed that a cancer was never spontaneously cured. This belief applied equally to the primary growth and also to the metastases. It was generally accepted, if even the smallest portion of the cancerous growth remained in the tissues, that it was sure to continue to grow and to form a recurrence. In a case which was believed to be cancer, either the primary tumor, or a portion of it which was known not to have been removed at an operation, disappeared, its disappearance was considered sufficient proof that the original growth was not a cancer. In fact, the definition ordinarily given of a cancer included a statement that it showed no tendency to spontaneous healing. It is now generally accepted that spontaneous healing of a primary malignant tumor does occur, though these cases are certainly rare.

There are several factors that are known to influence the spontaneous cure of cancer. The degree of malignancy of the growth is an important factor. For example, more cases of spontaneous cure of the mildly malignant epithelioma of the face seem to occur than of the more malignant cancers, such as occur in the breast. In general, the smaller the amount of tumor tissue left the greater is the chance of spontaneous healing. This is seen especially in incomplete operations. The smaller the amount of malignant tissue that remains after an operation the more likely is a spontaneous cure of this tissue to take place.

The type of tumor has also an important bearing on the subject of spontaneous cure of malignant growths. It is undoubted that more cases of sarcoma than carcinoma

undergo spontaneous cure. Sarcoma is a tumor that is sometimes not easily diagnosed even by a microscopic examination. The histological structure of it closely resembles that of other lesions, and an error in diagnosis is not infrequent. In different laboratories the same specimen is diagnosed differently. This is well illustrated in the different percentages of sarcomatous degeneration of fibromata of the uterus that are reported by different observers, even though sufficiently large series of cases are considered to minimize the element of chance. Some observers find only 1 or 2 per cent. of such cases and others report 8 or 10 per cent. Sarcomata vary even more than carcinomata in the degree of malignancy. Some cases, though undoubtedly sarcomata, are of slight degree of malignancy. All of these factors have an influence in the greater frequency of spontaneous healing of sarcomata than of carcinomata.

The spontaneous cure of cancer is best considered separately for the three conditions: (1) metastases; (2) incomplete operations; (3) primary tumors.

Metastases.—The spontaneous cure of metastases is probably most positively demonstrated in cases of malignant papillomata of the ovaries. In the early stages of this disease there is a cyst wall with papillomatous outshoots in the interior. Later either by spontaneous rupture or by penetration of the cyst wall there is a tumor covered on its external surface by the papillomatous growths. Still later there is an accumulation of fluid in the peritoneal cavity, and the peritoneum is covered seemingly everywhere by innumerable papillomatous metastases. In many of these cases the removal of the primary tumors is followed by the disappearance of the papillomatous metastases on the peritoneum. This is proved not only by the disappearance of the ascites previously present and the subsequent health of the patient, but also in numerous cases by direct inspection of the peritoneal cavity at a second operation performed for hernia or some entirely new lesion in the abdomen.

The cases of this type are so frequent that they have been seen by most abdominal surgeons, and demonstrate conclusively for malignant papilloma of the ovary, which is a malignant growth, though its malignancy is distinctly different than that of other forms of cancer, that its metastases may undergo spontaneous cure.

The cases of malignant papillomata of the ovary in which spontaneous cure of peritoneal metastases most frequently occurs are those in which the peritoneum is covered by a large number of minute metastases and in which there are no large metastatic growths. It is possible that these cases of peritoneal metastases illustrate a similar, though more minute, condition that exists in all malignant growths. It is probable, from all malignant growths that have attained definite size, that cancer cells are given off and are lodged in the neighboring vessels or tissues where they may become engrafted or maintain an independent existence. These minute aggregations of cancer cells undoubtedly in many cases are destroyed, as has been seen in cases of peritoneal metastases in malignant papillomata of the ovaries.

The way in which these small metastases are cured can be discussed only theoretically. It is known that the cancer cell is relatively a weak cell. It is destroyed by substances that will not interfere with normal tissue cells. It is probable that there exists in the body, possibly developed by the cancer itself, a substance which is antagonistic to the cancer cell, and that this substance is present in sufficient quantity to overwhelm single or small groups of cells, but insufficient to destroy large masses. Such an explanation, however, is entirely theoretical and does not give any real insight into the manner by which the cells are destroyed.

The spontaneous cure of malignant metastases in the *lymphatic glands* has various clinical proofs. The microscopic proof is more positive, but more difficult to obtain.

In the early stage of a malignant growth, as has already been stated, it is probable that many cancer cells are given

off which may become lodged in the tissues or which may be carried to the neighboring lymphatic glands. It is possible in the early stages that many such cells are destroyed in the glands in the same way that other foreign elements are destroyed. If the axillary glands, in cases of carcinoma of the breast, or the iliac glands, in cases of carcinoma of the cervix uteri, are examined, they are often found enlarged and hyperemic, though no malignant growth is present in them. This condition is sometimes looked upon as an inflammatory enlargement. It is probable, however, that the hypertrophy, in part at least, is due to the reaction resulting from toxins or cells carried to the lymphatic glands from the primary growth. The hypertrophy of the lymph nodes in the vicinity of a malignant growth may be considered as practical proof or as an intimation of the destruction of cancer cells in the glands.

If a gland is removed and found on examination to contain a malignant growth it is probable that other enlarged glands in the immediate vicinity are involved in the same manner. The only positive proof, however, is the microscopic examination, and this is possible only by removal of the gland. There is little doubt, however, if enlarged glands that are removed are found to be malignant, that similar glands that are not removed, particularly if hard and indurated, are similarly involved.

There are numerous cases reported in the literature, in which glands of this kind were left at the time of the removal of the primary malignant growth, and which disappeared, as shown by the subsequent course of the disease. For example, Peterson quotes a case of Beck's, of resection of the pylorus of the stomach for carcinoma, leaving carcinomatous glands in the vicinity. Three years later, at autopsy, these glands were found to be free of malignant growth, though there was a carcinoma of the sigmoid flexure. Such a case as this demonstrates the spontaneous cure of malignant metastases in lymphatic glands. Similar cases are sufficiently frequent in the

literature to furnish definite clinical evidence that such cures are probably of frequent occurrence.

Only a theoretical explanation of the spontaneous cure of these metastases can be given. The removal of the primary growth removed the source from which there was probably a constant flow of toxins and cancer cells in sufficient quantity to overtax the power of resistance of whatsoever nature it may be that existed in the lymph nodes. After the removal of this excess tax on the lymph nodes they are able to destroy the cancer cells that had already started to grow in the gland. Of the real nature of these toxins, as well as of the resisting power of the lymphatic glands, we have as little knowledge as we have of other phenomena of cancer growth.

There are other clinical observations which are advanced as evidence of the spontaneous cure of malignant metastases in lymphatic glands. The radical vaginal operation for carcinoma of the cervix uteri, as performed in the Schauta Clinic, does not include the removal of the iliac glands, as is done in the radical abdominal operation for the same condition as performed in the Wertheim Clinic, yet the number of recurrences following the vaginal operation is practically no greater than following the abdominal operation. It is claimed by some observers that this indicates that, following the vaginal operation, the diseased iliac glands frequently undergo spontaneous healing. This, however, is weak and uncertain evidence of the spontaneous cure of the cancerous metastases. The lymphatic glands in cases of carcinoma of the cervix uteri that are suitable for the radical vaginal operation are frequently not involved by the malignant disease. Furthermore, there may be certain technical advantages in the radical vaginal operation that offset the advantage in the radical abdominal operation of removing the iliac glands.

Examples of the spontaneous cure of malignant metastases in internal organs occur in the literature. Schmidt reported a metastasis in the lung from a gastric carcinoma,

in which a definite retrograde process was seen. The spontaneous cure of metastases in internal organs and in the bones is less frequent than in the lymphatic glands. The amount of malignant tissue in metastases in lymphatic glands is smaller than in most organs, and doubtless the smaller the amount of malignant tissue the greater is the chance of spontaneous healing. The function of the lymphatic glands seems to be to fight and destroy any foreign elements that reach them and to act as barriers for the protection of the system as a whole, and it is probable that their power of resisting and destroying cancer cells is greater than that of other organs.

Incomplete Operations. — Positive cases of the spontaneous cure of cancers are seen following incomplete operations for malignant growths. Usually following an incomplete operation, the cancerous growth increases with greater rapidity, due probably in part to exposing the fresh wound surface on which cancer cells become implanted and in part to forcing cancer cells mechanically into the tissues by the manipulation of the growth during the operation. That these are the causes of the increased rapidity of growth, usually seen after an incomplete operation, is confirmed by the absence of such increased rapidity of growth, if the malignant tumor is incompletely removed or destroyed by the cautery. In destroying a growth with a cautery, fresh wound surfaces on which cancer cells might become implanted are not made, and there is also less manipulation of the growth.

As an incomplete operation usually increases the rapidity of the growth, and a spontaneous cure of the malignant tissue not removed is a rare occurrence, partial operations should be avoided. When necessary to remove a part of the inoperable growth to relieve symptoms, if possible, the cautery should be used.

As examples of the spontaneous cure of cancerous tissue following the partial removal of the primary growth, Czerny reported two cases of incomplete operations for carcinoma of the large intestines, which were well at the

end of four and five years. Theilhaber reports a case of Rotter, of a young woman with a malignant adenoma of the rectum which returned after operation. The recurrence subsequently disappeared spontaneously and was not found at autopsy three years later.

The cases of disappearance of a malignant growth, following the use of the cautery or caustics by which malignant tissue was not completely removed, should not be considered cases of spontaneous cures. The work of Byrne, twenty years ago, and the more recent work of Percey have shown that the effect of cauterizing extends deeply into tissues and destroys cancer cells. The same is true of caustics even though they have of late properly fallen into disrepute.

Primary Tumor.—The spontaneous cure of the primary tumor is of less frequent occurrence than that of metastases or of portions of the growth which are left after partial removal of the primary growth. Though exceedingly rare, there are well-authenticated cases in which it has occurred.

The most frequent way in which spontaneous cure occurs in the primary malignant growth is by sloughing. Not infrequently polypi of the cervix uteri or of the intestine are found to be malignant without involvement of the organ to which it is attached. If such a polyp were to slough away, as any polyp is liable to do, it is easy to understand that the malignant growth is spontaneously cured.

Another example of the cure of a malignant growth by sloughing is that of cancer of the face that disappeared and did not return after an attack of smallpox.

The cases that are cured in this way by sloughing or by necrosis are examples of spontaneous cures in the sense that they occur without outside interference. They result, however, from the accidental destruction of the growth and the process is in no way different than the destruction of the growth by any other means, and it is not to be compared with the spontaneous healing

of malignant metastases or cancerous tissue that is left at an incomplete operation that has been described.

Similar cases of the spontaneous cure of primary malignant tumors do occur. For example, Czerny reported a case of inoperable carcinoma of the cervix uteri which became infected with erysipelas and was cured. The patient was well and free of recurrence at the end of five years. Czerny also has reported the disappearance of a recurrence of a carcinoma of the breast after an attack of erysipelas. The reason for the disappearance of the malignant growth following an attack of an infectious disease is not known. It has been suggested that the high temperature kills the weak cells of the growth. Under certain conditions the toxins of the infectious disease seems to exert a destructive influence on the cancer cells. This has given the hope that a serum containing these toxins may be made that will have a curative action in cases of carcinoma. Sera made according to different formulæ have been extensively used, and definite claims have been made of successful results. The results generally obtained by the use of these sera, however, have not been sufficiently successful to have them universally used. It is possible that the future will produce a serum that will have a result in cancerous conditions that is comparable to that obtained by salvarsan in syphilitic diseases.

A change in the local conditions without any attempt at removal has been followed by a spontaneous cure of the primary cancerous growth in a number of cases. This is most frequently seen in the gastro-intestinal tract, and a number of cases of the disappearance of the primary tumors following palliative operations are reported. For example, Czerny reports cases of carcinoma of the stomach which were treated by gastro-enterostomy and in which the primary tumor disappeared. There is in these cases a doubt regarding the diagnosis.

There is still another class of cases of spontaneous cure of primary malignant growths which appears in the

literature. This class includes cases that have all the clinical appearance of malignant tumors, and are diagnosed as such by thoroughly competent observers, but which, after reaching a certain stage of growth, cease growing, decrease in size, and ultimately disappear. These cases are so extremely rare that their occurrence at all is doubted by some observers, and an error in diagnosis is urged to explain their disappearance.

There seems to be no doubt that cancer cells may remain quiescent in the tissues for years, as is seen in cases of late recurrences. There is also no doubt, as has already been described, that cancerous tissue following incomplete operations, and malignant metastases, may be spontaneously cured. Cancer on the face has been observed to partly heal. Such observations as these, that is, the inactivity of cancer cells for a period of years, the spontaneous cure or partial healing of a malignant process, demonstrate conclusively that there exists in the system a definite resistance and destructive action to the growth of the cancer cells. By analogy to other diseases, it is probable that some individuals possess this power to a greater extent than others. It is fair to assume theoretically with all conditions favorable, that is, with an individual with special resistance to the growth of cancer cells, with a primary growth of a small degree of malignancy, with other conditions of which at present we have no knowledge, that a primary malignant growth may undergo spontaneous cure. Some of the cases that are reported in the literature were seen by careful observers, the diagnosis was made by a microscopic examination and the completeness of the cure was confirmed by autopsy after death from other causes. More positive and convincing clinical histories are rarely obtained. It must therefore be accepted that the spontaneous cure of primary malignant tumors do occur even though they are extremely rare. No case should be considered as such a cure unless the diagnosis was made by a microscopic examination by a competent pathologist,

and the cure demonstrated by an autopsy or the lapse of a long period of years.

Spontaneous cure of primary sarcomata undoubtedly occurs more frequently than of carcinomata.

MULTIPLE PRIMARY CANCERS.

There is nothing in a malignant tumor, either a sarcoma or a carcinoma, so far as is known, that protects the individual from another cancer. As a matter of chance, therefore, multiple primary malignant growths should be expected. Just as it is possible to have existing in the same person two benign tumors which have no relationship to each other, such as a lipoma of the back and a fibromyoma of the uterus, so also a combination of a benign and a malignant or two or even more malignant growths may be present at the same time in the same individual. There may be a sarcoma and a carcinoma or two sarcomata or two carcinomata in the same patient or even in the same organ. This is all a matter of chance. Multiple benign tumors of the same or different types are more commonly seen than multiple primary malignant tumors, because benign tumors are more common than malignant tumors, there are many more varieties and their duration is longer. The duration of a malignant tumor is relatively short.

Care must be taken to distinguish between multiple primary malignant growths and metastases. If the malignant tumors are of different histological structure, for example, if one is a sarcoma and the other a carcinoma, or if one carcinoma is composed of squamous and the other of cylindrical cells, there is no question that they are independent primary malignant growths.

If two malignant growths have the same histological structure each may be a metastasis from another tumor, which is giving no symptoms and cannot be diagnosed. In fact, the primary lesion may be so overshadowed by

the symptoms and courses of the secondary growths that it may never even be suspected.

There are reported in the literature numerous authentic cases of multiple tumors of the same histological structure which were undoubtedly both primary growths. It is probable that these cases are more frequent than is generally suspected, and as the reported cases would indicate.

Some cases of multiple primary malignant growths are the result of the same etiological cause. Excellent examples of such growths have been seen, and microscopically demonstrated, in the cutaneous cancer of workers in tar, paraffin, soot, etc. In these cases the same irritation, under the same conditions, naturally produces the same result—epithelioma. Williams reports such a case in a worker in asphalt who developed three independent malignant growths on the face, two of which were epitheliomata and the third a cylindrical-celled carcinoma from a sweat gland. Similar multiple primary malignant growths of the skin are reported which result from multiple lesions of the skin. Steinhauser reports such cases. Hutchinson reports cases of multiple rodent ulcers.

Cases of primary sarcomata of the skin, which, so far as is known, are primary growths, are described in books on dermatology as idiopathic multiple pigmented sarcomata. These cases may be multiple metastases from a single primary growth.

In the *uterus*, multiple tumors of the same histological structure cannot positively be demonstrated as primary growths, though it is possible that they may be. If, for example, there is a columnar-celled carcinoma of the cervix and also one of the fundus, one is probably secondary to the other. Cases are reported of carcinomata of different varieties occurring in the cervix and fundus uteri. Gellhorn describes such a case. Young and others report cases of carcinoma of the uterus and breast. Schminche reported a case of carcinoma of the gall-

bladder and sarcoma of the uterus. Emanuel reported a case of carcinoma and sarcoma in the same uterus.

In the *breasts*, as in the uterus, if the growths are of the same histological structure the chances are that one is secondary to the other. Carcinoma of both breasts occur in 1 or 2 per cent. of the cases, but one is probably secondary to the other. Williams reports a case of bilateral cancer and refers to others.

In the *gastro-intestinal tract*, multiple primary malignant tumors, according to Williams, are more frequent than in any other part of the body excepting the skin. Different parts of the gastro-intestinal tract have the same chronic irritation and possibly also the same polypi, and the multiple primary malignant growths are the natural results. Even though the histological structure of these tumors is the same, if the case is seen at an early stage, and before there is a general carcinosis, they can properly be considered multiple primary growths. Metastases from a malignant growth in the intestinal tract do not usually occur in other parts of the mucous membrane of the intestine in the early stage. In addition to these multiple tumors of the same histological structure, there are various different varieties reported. For example, Frangenheim reported a case of sarcoma and carcinoma of the esophagus. Bushnell and Hinds reported cases of carcinoma of the stomach and sarcoma of the ovary.

Malignant and Benign Tumors.—These occur frequently together, and the association is usually of little practical importance. If a malignant growth exists in an organ, and there is also a benign tumor in another part of the body, they are not considered to be related in any way, and one is not influenced by the other. This association of benign and malignant growths in different organs is so common in the experience of all surgeons, that no cases will be quoted from the literature.

If the benign and malignant tumor are both in the same organ, then the association is of more interest, because it raises the possibility that in some cases the

malignant growth is the result of the benign tumor. For example, the benign polyp of the rectum is frequently in some cases the antecedent of the malignant growth. The relationship of benign to malignant tumors has, however, been considered elsewhere.

REFERENCES.

Bruns' Beiträge, 1894, Bd. xii, S. 501.
Bushnell and Hinds. Zeit. f. Kreb., i, 3, S. 184.
Emanuel. Zeit. f. Geb. u. Gyn., Bd. 34, S. 1.
Frangenheim. Arch. f. Path. Anat., Bd. 184.
Gellhorn. Zeitsch. f. Geb. u. Gyn., 1897, Bd. 36, S. 430.
Hutchinson. Archives of Surgery, 1891, iii, 318, 335.
Mandry. Beiträg. z. klin. Chir., 1892, Bd. viii, S. 589.
Petersen. Beitr. z. klin. Chir., 1902, Bd. 32.
Richter. Wien. klin. Woch., 1905, S. 865.
Schminche. Arch. f. Path. Anat., 1906, Bd. clxxxiii, S. 160.
Trans. Path. Soc., London, 1905.
Williams. Diseases of the Breast, 1904, p. 302, etc.
Williams. Twentieth Century Practice of Medicine, xvii, 228.
Young. Archives of Middlesex Hospital, 1904, iii, 165.

CHAPTER V.

CARCINOMA AND SARCOMA OF THE BREAST.

CARCINOMA OF THE BREAST.

Frequency.—In the United States registration area in 1912, which included approximately 63 per cent. of the entire population, there were 4431 deaths recorded from malignant tumors of the breast. For the entire United States in the same proportion there would have been slightly over 7000 deaths from cancer of the breast, or about 10 per cent. of all cancer deaths. Of the females who died of cancer, the breast was involved in 15.1 per cent. of the cases.

Williams, in the study of the mortality returns for England and Wales, found 15.8 per cent. of the cancer deaths of females due to cancer of the breast.

In the Middlesex Hospital, as reported by Campiche and Lazarus-Barlow, cancer of the female breast constituted 21.78 per cent. and of the male breast 0.29 per cent. of malignant disease of all organs. Of cancer in females alone, the breast was the organ involved in 35.29 per cent.

The difference in the percentage of deaths in mortality records, approximately 15 per cent. of females, and that for hospital cases, approximately 35 per cent. of females, is explained by the location and relative ease with which carcinoma of the breast is recognized. Cancer of more obscure origin is recognized later and those affected apply less frequently for hospital treatment, but ultimately are recorded in mortality statistics.

Age.—The following table gives the percentages by age groups of the cases that died of cancer of the breast as reported in the United States registration area for 1912:

20 to 29 years	0.9 per cent.
30 to 39 "	8.0 "
40 to 49 "	20.0 "
50 to 59 "	27.0 "
60 to 69 "	20.0 "
70 to 79 "	15.0 "
80 to 89 "	6.0 "

The following table, adapted from Judd and Sistrunk, gives the ages by decades of 651 cases at the Mayo Clinic:

20 to 30 years	2.0 per cent.
30 to 40 "	22.0 "
40 to 50 "	35.0 "
50 to 60 "	22.0 "
60 to 70 "	14.0 "
Over 70 "	4.0 "
	99.0 "

These tables confirm the usual observations that cancer of the breast is rare under thirty years and most frequent at about fifty years of age. It will be noticed that one table is of mortality records and the other from hospital records. There are a few cases reported in the literature under the age of twenty-five years. Handley states that it is unknown before puberty.

Sex.—About 1 per cent., or slightly less of the cases of carcinoma of the breast, occur in males.

Civil State.—As recorded in the Middlesex Hospital Reports, of 1000 female patients with cancer of the breast, 77.2 per cent. were married and 22.8 per cent. were unmarried. It was estimated that this ratio was approximately the same as the proportion of married and unmarried females over twenty-five years of age in the general population during the same period. The ratio of married to unmarried women in cases of cancer of the

breast, as determined by other observers is somewhat higher than that in the Middlesex Hospital. Schwartzkopf in 395 cases found 86.5 per cent. married, and quoted eighteen other observers with an average of 83 per cent. of cases in married women.

If the percentage of married and unmarried women among the cases of cancer of the breast is the same as it is among women in the general population, as was reported in the *Middlesex Hospital Reports*, then married women are no more subject to cancer of the breast than single women. This would mean that acute and chronic mastitis, lactation, etc., which are present in married women, exert no influence in the development of cancer of the breast. It is generally accepted that various conditions in the breast, directly or indirectly the result of child-bearing, do favor the development of cancer, and that there is a larger percentage of married women among the cases of cancer of the breast than in the general population.

Mastitis.—Schwartzkopf reported that 10.7 per cent. of all cases and 22 per cent. of those who had children, in his series gave a history of mastitis. These figures in themselves are not absolute proof of the influence of mastitis in the development of cancer, as the frequency of mastitis in non-cancerous cases is not known, but it undoubtedly is considerably less than the percentages given above.

A further observation in Schwartzkopf's series, which is of greater significance in showing the undoubted influence of the mastitis in the development of carcinoma of the breast is the frequency with which the carcinoma developed in the same breast as the mastitis. If the mastitis did not influence the development of the carcinoma, the two lesions would not so frequently have involved the same breast.

In Schwartzkopf's series the average period between the mastitis and the carcinoma was 12.8 years; the extremes were four months and thirty-eight years. The

long period between the mastitis and the development of the carcinoma would indicate that the scar from the mastitis was the causative factor.

Errors of Lactation.—Leaf, in an analysis of 73 cases of carcinoma of the breast who had borne children found that 2 cases had nursed normally, 10 cases had not nursed at all, 1 case had deficient milk supply, in 21 cases there was overlactation on one or more occasions, in 8 cases there was underlactation on one or more occasions, and in 30 cases there was both overlactation and underlactation in different pregnancies.

It is not easy to determine always what constitutes an error in lactation. It would seem, however, as Leaf maintained, that the number of cases in his series in which lactation had been abnormal was higher than would be expected in general.

Leaf believed that overlactation would so damage the secretory cells that there would be an increased disposition to the development of cancer. Also, that by underlactation, the retention of the milk in the breast, would act as an irritant to the secretory cells and favor the development of a malignant growth. This, however, is largely theoretical, and further observations must be made before the real influence of errors in lactation can be determined.

Chronic Cystic Mastitis.—This disease of the breast is most frequent between the ages of forty and fifty years, and is common between the ages of thirty and sixty years; that is, the ages during which it is most frequently found corresponds to the ages of greatest frequency of cancer of the breast. The disease has been described by various writers, and a large number of different names have been applied to it. By some it is believed that the formation of cysts is the result of a chronic inflammation. It may occur in only one or in both breasts, it is probably more frequent in married than in single women, and, as has been stated, it is most frequent at the menopause. As causes of chronic cystic mastitis, are given various influences which interfere

with the normal functions of the breast, such as acute mastitis, abnormal lactation, menstruation, etc.

Etiology.—Many of the etiological factors of chronic cystic mastitis are the same as those of carcinoma of the breast, and there is a close relationship between the two diseases. The tendency of chronic cystic mastitis is to advance and to involve more and more of the breast. With the formation of more cysts there is also a tendency to proliferation of cells. This is sometimes so to such an extent that some writers have considered it a true neoplasm, and have assigned to the lesion the name of a neoplasm.

In this connection, as elsewhere, it is not possible to state absolutely that the carcinoma is the direct result of the chronic cystic mastitis, and would not have developed if the chronic cystic mastitis had not previously existed. The relationship between the two diseases, however, is such that there is greater evidence that chronic cystic mastitis does influence the development of a cancer of the breast than there is of many of the etiological factors given for carcinoma in this and other organs.

The frequency with which carcinoma ultimately develops on chronic cystic mastitis cannot be determined definitely. Warren found carcinoma associated with the chronic cystic mastitis in 13 per cent. of his series. This, however, gives the frequency with which carcinoma was associated with the chronic cystic mastitis at the time the removed tissue was examined. It does not indicate the additional cases that would have developed if the chronic cystic mastitis had not been removed. Judd states "that many of the best authorities believe the condition occurring in women of the cancer age will become malignant in more than half of the cases."

This evidence should indicate two things in the treatment of chronic cystic mastitis. In a woman of the cancer age, chronic cystic mastitis should be removed as a precancerous lesion, and should always be examined at once, to discover if there is any malignant tissue associated

with it, so that a radical operation can be done if it is found necessary.

Diagnosis.—The diagnosis of chronic cystic mastitis is not difficult, but it is impossible to positively exclude a malignant change in it, excepting by a microscopic examination after it has been removed. The examination should be thorough, and include all parts of the tissue removed.

Trauma.—The breast is an organ so placed that it is exposed frequently to injury, and it is not strange, therefore, that a history of definite traumatism is frequently obtained in cases of carcinoma of the breast. This traumatism may be a single one, or may be repeated slight injuries, as from poorly fitting corsets or carrying weights against the chest.

At the Middlesex Hospital there was a history of injury to the breast in 18.7 per cent. of all cases of mammary carcinoma. Leaf reported history of injury to the affected side in 32 per cent, of the cases. In the series of Schwartzkopf there were 34 cases, or 8.8 per cent., with a history of injury. The varieties of injuries which he recorded include blows, sting of wasp, prick of needle, etc. The average percentage of cases that gave history of trauma of twenty-one authors reported by Schwartzkopf was 9.2 per cent.

The interval of time between the injury and the first symptoms of the cancer of the breast varied from two months to twenty years. In 13 of the 34 cases the interval was less than two years.

Trauma is proportionately more frequently an etiological factor in carcinoma of the male than of the female breast.

Pathology.—The *scirrhus carcinoma* is made up largely of fibrous tissue, with scattered areas of cancer cells. The growth is hard and nodular, and early becomes adherent to the skin or to the pectoral fascia. The scirrhus carcinoma of the breast does not ulcerate at all or only late in the disease. The contraction of the fibrous bands produces the puckering of the skin and the retraction

of the nipple. On section the growth is sufficiently hard to offer considerable resistance to the knife.

The *medullary carcinoma* of the breast grows more rapidly than the scirrhus, forms a larger tumor, and frequently ulcerates, forming a fungus growth. The growth is made up more largely of cellular elements than the scirrhus variety. On section, the growth is soft and may offer little resistance to the knife. Though the growth is not encapsulated, there is a distinct outline between it and the normal breast tissue.

Between the medullary and the scirrhus types there are all variations; even in different parts of the same tumor different varieties may be found.

Location.—The location of the primary growth in 1010 cases of carcinoma of the breast as reported in the archives of the Middlesex Hospital and of 177 cases reported by Schwartzkopf is given in the following table:

	Middlesex hospital.	Schwartzkopf.
Beneath the nipple	12.2 per cent.	
In the nipple	7.6 "	
Superior and outer quadrant	44.9 "	46.89 per cent.
Superior and inner quadrant	16.7 "	15.82 "
Inferior and outer quadrant	12.4 "	27.12 "
Inferior and inner quadrant	6.2 "	9.6 "
	100.0 "	99.43 "

It will be noticed that about one-half of all the cases began in the upper and outer quadrant.

Side Affected.—It is probable that carcinoma of the breast involves the right and left breast with about equal frequency. In the Middlesex Hospital in 1512 cases the left breast was involved in 777 cases, and the right in 735 cases. In Schwartzkopf's series of 395 cases the left breast was involved in 197 cases and the right in 198 cases. The difference in each of these series is too small to consider that carcinoma occurs more frequently in one breast than in the other. Other observers have found a slight difference in favor of the right breast. Observers

who have believed that the right breast is involved more frequently have explained it by the greater use of the right arm. Those who believe in the greater frequency of involvement of the left breast explain it by carrying the child more frequently on the left arm. The influence of these etiological factors cannot be great and their difference even less. The statement that has been made that one breast is involved with approximately the same frequency as the other is the best decision that can be made from our present evidence.

Both Breasts.—Both breasts are found involved by carcinoma in a few cases; for example, in Schwartzkopf's series both breasts were involved in 4 cases in a total of 395 cases. There are two ways by which the occurrence of carcinoma in the two breasts can be explained. One explanation is that a carcinoma develops in each breast at practically the same time, each growth entirely independent of the other. The other explanation is that one growth is a metastasis from the other. This is probably the correct explanation of most cases. Theoretically there is no reason to deny the possibility of a carcinoma starting simultaneously in each breast, and when the frequency of carcinoma of the breast is considered the chances are in favor of such an occurrence. Campiche and Lazarus-Barlow state, "Not a single *indubitable* instance of primary cancerous growth originating separately in both breasts is recorded at the Middlesex Hospital." Rodman is of the opinion that one breast is always affected before the other, and that the second breast is involved by metastasis from the first.

It is well at this point to consider the frequency with which the second breast is involved by a metastatic growth, either late in the course of the disease in inoperable cases or in cases following operation. At the Middlesex Hospital in 1512 cases there was a secondary involvement of the other breast in 137 cases, or in 9 per cent. In 35 of these cases, in which the point was recorded, the interval between the beginning of the primary growth and the

involvement of the second breast was, on the average, three years. Rodman quotes Rotter, that in 35 recurrences 6 were in the opposite breast.

The usual explanation of the involvement of the second breast is that it takes place through the lymphatics beneath the skin or by the anastomosis of the lymphatics of the two sides in the anterior mediastinum. Handley believes that the involvement of the second breast is by the permeation of the malignant growth along the lymphatic vessels across the middle line.

Extension of Carcinoma of the Breast.—As with carcinoma in other parts of the body, that of the breast extends largely through the lymphatic vessels, and involves the lymph nodes, organs, bones, etc., in remote parts of the body. It also spreads by direct extension, and through the bloodvessels. The permeation theory advanced by Handley is described later. A better understanding of the ways by which carcinoma of the breast spreads has greatly improved the operative results of the disease.

Lymphatic Glands.—The lymphatic vessels of the breast run in four directions, and extension of carcinoma takes place in each one of them. The *largest number* extend to the axillary glands. This is true of the superficial and also of the deep lymphatics, and of the inner as well as the outer part of the breasts. From the axillary glands the supraclavicular and cervical glands may be involved. A *second set* of lymphatic vessels, probably only superficial ones, pass upward over the clavicle and involve the supraclavicular glands directly without first passing through the axillary glands. There are only a few of these lymphatic vessels, and the supraclavicular glands are not frequently involved in the carcinoma of the breast, excepting at the late stage of the disease, and when they are diseased it is usually indirectly through the axillary glands. *A third set* of lymphatic vessels pass to the lymphatic glands in the anterior mediastinum. It is probable that they intercommunicate with the opposite side, and that it is through these channels that the second

breast is sometimes involved. This is on the theory that when there is a carcinoma in each breast, one is primary and the other secondary, and not that both are primary growths. Fortunately, there are not many of these vessels, and early involvement of the mediastinal lymph nodes is rare, as these glands are beyond the reach of our present diagnostic and operative technique. At the Middlesex Hospital the bronchial and mediastinal glands were found at autopsy to be involved in 17 per cent. of 470 cases. The *fourth set* of lymphatic vessels are those that pass directly across from one breast to the other. These lymphatic vessels are also few in number, but may be the channel through which the other breast is secondarily involved.

Of these four sets of lymphatic vessels the one that leads to the axillary glands is the largest, and drains all parts of the gland. The condition of the axillary glands is an important diagnostic help with tumors of the breast, and their routine removal is a part of the technique of all modern operations for carcinoma of the breast. Ultimately, if the course of the disease is not checked, they are involved in most cases. At the Middlesex Hospital in a series of 470 cases which came to autopsy, the axillary glands were found involved in 75 per cent. of the cases. In 9 per cent. the axillary glands of both sides were involved.

It would be of distinct value if the period of the disease at which the axillary glands are generally first involved could be determined. It would, of course, not be the same in all cases. In an analysis of 500 cases at the Middlesex Hospital "a lump" in the axilla was the first symptom of carcinoma of the breast that was noticed in 2 per cent. of the cases.

Schwartzkopf found in 12 cases, in which the history seemed sufficiently reliable to be of value, that the average interval between the first sign of a tumor in the breast and an enlargement of the axillary glands was 7.46 months. The number of cases in this series is small and, as Schwartzkopf himself points out, the source of the information

must necessarily be of a nature that its accuracy is uncertain.

Viscera.—The following table gives the frequency with which metastases were found in different organs in 470 cases of carcinoma of the breast which came to autopsy at the Middlesex Hospital:

Liver	45.0 per cent.
Lungs	35.0 "
Parietal pleura	35.0 "
Kidneys	9.0 "
Adrenals	7.0 "
Ovary	5.0 "
Brain	5.0 "
Stomach and intestines	3.0 "
Pancreas	3.0 "
Spleen	2.5 "

The liver is the organ most frequently involved by the metastatic growth in carcinoma of the breast. This occurs probably in most cases through the general lymphatic and blood circulation. In part also through lymphatic vessels that accompany the vessels of the rectus muscles and enter the liver through the triangular ligament.

The lungs and pleura are involved less frequently than the liver, though they are in close relationship to the breast. The lungs and pleura may be involved through the general lymphatic and blood circulation, or from the mediastinal, infraclavicular, or supraclavicular glands, that may have received the infection directly from the breast. In other cases there may have been a direct extension of the growth in the breast through the thoracic wall to the pleura and lungs. In some cases the extension is from the lungs to the pleura.

Bones.—The osseous system seems to be more frequently involved in the secondary growths in carcinoma of the breast than in carcinoma of other organs. The following table gives the number of times various bones were found in 470 cases of autopsy for carcinoma of the breast at the Middlesex Hospital:

Ribs	41 cases.
Vertebral column	32 "
Femur	28 "
Skull	16 "
Humerus	15 "
Clavicle	9 "
Leg	2 "
Forearm	1 "

The ribs, sternum, and clavicle may be involved by direct extension from the primary growth in the breast. The humerus may be involved from the axillary glands. The involvement of the bones, excepting in cases where they are involved by direct extension, is probably through the blood system. It will be noticed by the table that the humerus and femur are involved more frequently than the bones of the forearm or of the leg, and most statistics agree with this observation. Rodman, however, does not accept this, and believes that the findings are due partly to incomplete autopsies and partly to the more frequent occurrence of spontaneous fractures of the femur and humerus than of the bones of the leg and forearm.

Permeation of Cancer.—It is universally accepted that carcinoma cells spread through the lymphatic vessels to the lymph nodes. The nodes may for a time filter out the cancer cells, but ultimately they pass the glands and reach the general blood system. There is no question that the carcinoma may grow directly into the lumen of a bloodvessel and that cancer cells may be washed off into the general circulation. This embolic method is the process that is generally accepted to explain metastatic growths in organs remote from the primary carcinoma. There are, however, certain recognized facts that are not satisfactorily explained by this theory. Handley has made an extensive study of the dissemination of cancer of the breast, and has explained it in part by what he has termed the *permeation* process. Handley, against an embolic process as an explanation of dissemination of cancer of the breast, raises the point that various organs

on the average should be attacked with the same relative degree of frequency if this was the result of an embolic process. The spread of cancer cells by an embolic process should affect various organs with the same relative frequency as those organs are affected in pyemia, which is also spread by an embolic process. Such, however, is not the case. For example, in pyemia the liver and the spleen are involved in the ratio of 3 to 2; in carcinoma of the breast the ratio is approximately 14 to 1. He also urges against the embolic theory that the same viscus is involved by a secondary growth with different degrees of frequency by carcinomata of different organs. That is, the liver is involved secondarily more frequently when the primary growth is in the breast than when it is in the uterus. Handley accepts the embolic process as one method by which cancer is spread, but believes the permeation process is of equal or greater importance, and must be accepted in order to explain certain faults in the embolic theory.

According to the permeation theory the cancer cells grow along the lymphatic vessels centrifugally from the primary growth. Handley describes this by the following illustration: Certain bacteria cannot be forced through a porcelain filter, but if they remain in it for a time they grow through its pores and can be detected on its outside. In the same way the cancer cells grow in the lymphatic vessels against the current of lymph. When the pressure of the growth is sufficient to overcome the wall of the lymphatic vessel it breaks through and sets up around it an inflammatory reaction. The result of this inflammatory reaction may be the destruction of the cancer cells and the lymphatic vessel is replaced by a fibrous band. Handley calls this the *perilymphatic fibrosis*. Instead of the cancer cells being completely destroyed, some may escape and form isolated carcinomatous nodules. The perilymphatic fibrosis never quite overtakes the permeation, so the disease continues to spread at the outer edge. There are, in this way, formed about the primary

growth, as a centre, three zones. In the outer zone the process of dissemination is extending centrifugally in a constantly enlarging circle. In the inner zone the process has been largely checked by the cancer cells being killed and the lymphatic vessels being replaced by fibrous bands by the perilymphatic fibrosis. In places in this inner zone there may be isolated carcinomatous nodules made up of cancer cells that have escaped destruction. In the middle zone, which is relatively narrow, the perilymphatic fibrosis is actually changing the outer active zone of permeation into the inner zone of secondary nodules and destroyed lymphatics. This is an interesting example of the local cure of a cancerous process.

In the early stage of the disease the outer edge of the zone of permeation is not far from the primary growth. As the disease progresses this zone of permeation increases in circumference and the edge may be, according to Handley, two feet from the primary growth, reaching to the scalp, the back, to the groins, and to the thighs. This growing edge can by proper examination be detected microscopically, but of course cannot be detected by other means.

By the permeation theory of the dissemination of cancer of the breast, Handley explains certain features that do not correspond to an embolic process. This is particularly true of subcutaneous nodules which occur in certain cases. Not infrequently the primary tumor in the breast is surrounded by a complete circle of subcutaneous nodules. In some cases, similar subcutaneous nodules are found in more distant parts of the body, though the thoracic or abdominal viscera are not involved. Such conditions are well explained by the permeation theory, and it is probable that these lesions are formed in the general way described by Handley.

The dissemination to the abdominal organs is also explained by Handley by the permeation theory. The lower and inner margin of the breast is close to the epigastric angle, and at this point the deep fascia in which the

carcinomatous permeation is progressing is close to the peritoneum. After the peritoneum, the upper surface of the liver through its serous coat is first involved, and later by gravitation the organs lower in the abdomen. This will explain the greater frequency with which the liver is secondarily involved in cases of carcinoma of the breast, and also the cases in which a number of the abdominal viscera are involved, but all the thoracic viscera have escaped. The permeation theory is not as generally accepted to explain visceral dissemination as it is to explain the subcutaneous nodules.

Handley also applies the permeation theory to the involvement of the osseous system. He believes that the bones are involved by secondary growths in about the order previously given from the Middlesex Hospital records. That is, that the bones nearer to the breast, the ribs, sternum, clavicle, vertebra, cranium, humerus, and femur are involved more frequently than the bones, such as the radius, ulna, tibia, fibula, and bones of the hands and feet, which are farther away, because they are reached sooner by the process of permeation.

Symptoms.—*First Signs.*—The following table gives the five most frequent first signs in an analysis of 500 cases at the Middlesex Hospital:

Growth in breast	315 cases	or 63.0	per cent.
Growth and pain	57 "	11.4	"
Pain alone	72 "	14.4	"
Retraction of nipple	19 "	3.8	"
Growth in axilla	10 "	2.0	"

One or another of these five symptoms is the first sign of a carcinoma of the breast in 95 per cent. of the cases.

Growth in the Breast.—This is the first symptom in three-quarters of the cases of carcinoma of the breast. Some writers state that it is the first symptom in a larger percentage of the cases. The growth in the early stage can be best felt with the palm of the hand, and it is in practically all cases single and it is movable. The hard-

ness which is characteristic of a carcinoma may be difficult to detect in the early stage when the growth is still small. Practically, in the early stage when the growth is still small, there is no way, other than by its removal and a microscopic examination, to determine whether a tumor of the breast is benign or malignant. The indication, therefore, is to remove every tumor of the breast in order to exclude the possibility of overlooking a malignant growth. The only exception to this rule is a tumor that is known to have existed for a long period and has shown no recent signs of activity, and tumors in women under the age that carcinoma is likely to occur. The duration of its existence may be sufficient to exclude its malignancy, but even if the growth is benign, its removal is probably the best treatment, as a malignant change may occur in the benign tumor. At the Middlesex Hospital between 1900 and 1904, of all tumors of the breast 89 per cent. were shown to be malignant. The part of the breast in which the growth occurs has already been given.

Pain.—Pain either alone or associated with a growth was the first symptom in 25 per cent. of the quoted cases at the Middlesex Hospital. This percentage is probably higher than that usually given. As a rule, pain is not an early symptom of carcinoma of the breast, and when present it is of a mild type. In the advanced stage of the disease the pain may be severe, and may be due to pressure on the brachial plexus or other nerves, to edema of the arm, or to secondary deposits in the bones or internal organs. Usually the presence of real pain indicates that the growth has passed the operable stage.

Retraction of Nipple.—This was the first symptom noticed in 3.8 per cent. of the 500 studied cases at the Middlesex Hospital. It was recorded as a symptom in 26 per cent. of all cases at that hospital. It is more frequently a symptom of carcinoma of the breast when the growth is situated near the nipple. It is usually not an early symptom when the growth is distant from the nipple. It may be present in other conditions than

carcinoma, and may be absent in carcinoma. The retraction of the nipple does not mean that the case is inoperable.

Probably most cases, in which retraction of the nipple is recorded as the first symptom, were patients who gave little attention to local conditions or whose breasts were so large that the growth could not easily be detected.

Axillary Glands.—The enlargement of the axillary glands is an important, though not usually an early symptom, of carcinoma of the breast. Schwartzkopf estimates that the interval between the first symptoms of the disease and the enlargement of the axillary glands averaged about six months. Enlargement of the glands in the axilla may be due to other causes than the growth in the breast. The enlargement of the axillary glands does not indicate that the growth has reached an advanced stage, nor that it is inoperable, though the prognosis is less favorable.

Discharge from the Nipple.—This may be brown, or bloody, or it may be cream color. A discharge from the nipple was the first symptom in 1.6 per cent. of the cases in the Middlesex Hospital series.

Dimpling of the Skin.—As the growth approaches the surface there is a change in the skin. In the early stage this change may be a dimpling or retraction of the skin, which is apparent to the eye, or can be demonstrated by manipulation. The dimpling of the skin is due to contraction or the formation of fibrous bands. At a late stage the skin becomes adherent to the growth, or the "pig-skin" appearance is seen. The sebaceous glands appear larger and may be especially marked by the accumulation of foreign matter in their orifices. The skin is thick and leathery, at first over the growth and later over most of the breast. This condition is most frequent in carcinoma, but may also be seen in other conditions, such as chronic mastitis, tuberculosis, and syphilis.

Edema of the Arm.—This is a late and an infrequent symptom of carcinoma of the breast, and is due to inter-

ference with the lymphatic vessels. This interference may be with the large lymphatic channels by the growth, or the destruction of a large number of the smaller vessels by the permeation process, as is described by Handley. At first the arm shows the usual signs of edema. The skin pits on pressure, the arm increases in size, and there is limitation of its motion. Later, there is further increase in the size of the arm, the skin is hard and brawny, and there is a constant severe pain.

Ulceration of the Breast.—This is a late symptom of the disease, and is becoming less frequent as patients seek relief earlier. At the Middlesex Hospital between 1897 and 1903, 22 per cent. of the cases were ulcerated at the time of admission. At that hospital it was found, on the average, that the disease had existed about two and a half years before the ulceration began.

Immobility of the Growth.—In the early stage, a carcinoma of the breast is freely movable. Immobility indicates that it has become adherent to the pectoral fascia. This occurs earlier in the deep-seated cancer than in the more superficially located growths. If the growth has become adherent to the pectoral fascia and is fixed, while it may not be absolutely inoperable, it has reached a stage when the chance of a permanent cure is relatively small.

Size of the Breast.—The size of the breast may be decreased by the contraction due to the growth even before there has been any ulceration. The size may also be decreased by the destruction of tissue due to the ulceration. In other cases, particularly in those of rapid growth, the breast may be considerably increased in size.

Treatment.—This is divided into the treatment of the operable and the inoperable cases. A case would be considered inoperable (1) if the growth is fixed to the chest wall, (2) if the involved lymphatic glands either in the axilla or the neck are fixed to surrounding tissue, (3) if there are cutaneous, visceral, or bony metastases. A case would be classified and treated as inoperable, if

there were a general constitutional disease which would soon terminate the life of the patient or would make an operation overhazardous.

Inoperable Cases.—The benefit of radium or *x*-rays is uncertain, but the use of either is entirely justifiable in cases of inoperable carcinoma of the breast, and either for the primary or any secondary growth. The external location of the breast makes a growth in it more accessible to the action of the rays than a growth in an internal organ, and greater benefit should therefore be expected from their use. The benefit obtained is by limiting the rapidity of the growth and the relief of the pain. It is doubtful if a case is ever cured by this means. Neither radium nor *x*-rays should be used on a case that is suitable for operation. The plan of first using radium or *x*-rays on an operable case previous to the operation is a waste of valuable time and should not be done. The use of *x*-rays after the operation with the object of destroying any cells that may have been left in the tissues has much more to recommend it, and is practised by some surgeons. The use of drugs for the relief of the pain of an inoperable carcinoma of the breast should be delayed as long as possible and the milder sedatives used first. It must be remembered that the duration of a case that is inoperable, or which has recurred, may be some months, or even years, and if the use of morphin is started too early the discomforts of a morphin habit will be added to that of the carcinoma. Toward the end of the disease there is no drug equal to morphin for the relief of the pain, and it should not be withheld from the patient.

Edema of the arm may be a troublesome symptom on account of pain and sometimes of paralysis of the arm. In the early stage of the disease, relief of the swelling and of the pain can be obtained by the position of the arm. The support of the arm in a sling may be of comfort to the patient. Later the pain may require the administration of morphin.

The treatment of the ulceration is largely that of clean-

liness. This may be accomplished by sterile water or by the use of antiseptics, such as peroxide of hydrogen. The object is partly to remove discharges which may be offensive to the patient and partly to avoid secondary infection, which would add to the general discomfort. In some cases, troublesome hemorrhages may result from the ulceration and require treatment.

Operable Cases.—If the local conditions of the growth and the general health of the patient are such that a radical operation, that is, the removal of the breast, pectoral muscles and axillary contents, can probably be successfully done, no other treatment should be considered, and the operation should be done with the least possible delay.

Skin Incision.—The area of skin removed must be liberal to avoid the skin metastases and local recurrences that are frequent. This is an important point in all operations for carcinoma of the breast. If the wound cannot be entirely covered by the skin at the end of the operation the remaining area can be skin-grafted.

Rodman believes that the favorable results obtained by Gross and by Banks, each curing about 21 per cent. of his cases, was due to the free removal of the skin, as neither removed the pectoral muscles and neither probably made as thorough an axillary dissection as is done today.

The subcutaneous or paramammary fat is removed from an area even larger than the skin. This is partly for technical reasons, the undermining of the skin allows it to come together more easily, and partly to remove the lymphatic vessels and glands from a larger area.

Axillary Contents.—The removal of the axillary glands as a part of the operation for carcinoma of the breast has been done since about 1875. Previous to that date the removal of the breast alone was the more frequent operation. At present the removal of the axillary glands with the surrounding fat, and as far as possible in one mass with the breast, is a necessary part of every operation for mammary carcinoma.

Supraclavicular Glands.—If these glands are diseased they should be removed. Some surgeons advocate their removal in all cases, but this is not generally accepted. If the supraclavicular glands are palpable, Judd removes one for microscopic examination. He states that his experience is "if the supraclavicular glands prove to be involved, that the patient lives longer and more comfortably if not operated upon." The middle ground, that is, to remove these glands if they are found to be diseased, is the more usual course followed.

Removal of the Pectoral Muscles.—Rodman gives to Volkmann the credit of first removing the pectoral muscles in operations for carcinoma of the breast. He apparently removed them only in the more advanced cases, but his results in these advanced cases with the removal of the pectoral muscles were more favorable than those of the less-advanced cases if the pectoral muscles were not removed.

Halsted was the first to advocate, as he did in 1894, the removal of the pectoral muscle in all cases, even if early ones. The removal of the pectoral muscles is a more extensive operation, allowing the removal of tissues which frequently contained diseased lymphatic vessel and glands. It also allows a more thorough dissection of the axillary contents and the removal of any diseased glands that may be in the space between the pectoral muscles posterior to the pectoralis major.

End Results.—*Mortality.*—With the improvement of general surgical technique the mortality following operation for carcinoma of the breast has steadily decreased. At present the operative mortality is probably about 1 per cent. The deaths that do occur are usually the result of surgical accidents, such as embolism or pneumonia, and not directly from the operation itself. The causes of death of 15 cases (4.6 per cent.) in Schwartzkopf's series were pneumonia (7), erysipelas (2), embolsim (2), hemorrhage (1), miscellaneous (2).

Permanent Cures.—At the Mayo Clinic, as reported by Judd, of 266 cases of carcinoma of the breast which could be traced, 39.8 per cent. were alive at the end of five years, though 6 cases had recurrences; 14 of the cases in the series had died of other diseases.

Schwartzkopf analyzed the results in his series of cases in regard to the local conditions. His results are estimated for a three-year period as a permanent cure. Of the cases the size of which was less than that of an egg, 34.26 per cent., of the size of an apple, 12.1 per cent., and of the size of a child's head, 5 per cent., were cured. Of the cases that were adherent to the skin, 17.2 per cent. were cured. Of the cases that were adherent to deeper structures there were no cures. Of the cases which had ulcerated, 20 per cent. were cured.

Schwartkopf divided his cases into three classes: (1) cases in which there were no palpable axillary glands, of which 80 per cent. were alive at the end of three years; (2) cases of moderate extent, that is, with involvement of the axillary glands, of which 20 per cent. were cured; (3) the most extensive cases, only 5 per cent. were cured.

Regarding the variety of the growth, Schwartzkopf found of the cases of carcinoma scirrhosa 44.7 per cent. and of carcinoma simplex 18.9 per cent. were living at the end of three years. Of 10 cases of carcinoma medullare none were cured.

Recurrences.—In a series of 82 cases of recurrences after operation, Schwartzkopf found that about 80 per cent. occurred during the first year following the operation. A number of cases of late recurrences are reported in the literature. Schwartzkopf reports one case that occurred at the end of eight years. Judd reports recurrences after five, six, nine, and twelve years, and speaks also of one reported by Matas at the end of twenty-five years and another of Ransohoff at the end of twenty years. Rodman believes that nearly all cases that are reported as late recurrences are not recurrences, but subsequent primary growths in cases that have shown special sus-

ceptibility to the disease. Carcinoma of the various internal organs is relatively frequent, and it is easier to believe that the carcinoma of the breast was permanently cured and that the internal organ was attacked by a primary growth, than to believe that cancer cells remained dormant for twenty years, and then commenced to grow. The same reasoning can be used for the cases of late recurrences in the scar. It may be a new primary growth and not a recurrence of the original growth.

SARCOMA OF THE BREAST.

Etiology.—*Frequency.*—Sarcoma of the breast is an infrequent growth. Rodman in a collection of 5000 tumors of the breast from reliable sources found that only 2.78 per cent. were sarcomata. In the Middlesex Hospital, as reported by Campechi and Lazarus-Barlow, up to 1905 only 45 cases of sarcoma of the breast had been recorded. Of these 45 cases, 43 were primary and 2 secondary growths.

Age.—Sarcoma of the breast may occur at any age, but is most frequent in middle life. Rodman in an analysis of 100 cases found that one-half occurred between the age of forty and fifty years. The youngest patient at the Middlesex Hospital was twenty-three years of age.

Trauma.—It is recorded that injury is a more frequent etiological factor in sarcoma than in carcinoma of the breast. This opinion is probably based more on the usual rule that sarcoma more frequently than carcinoma results from injury, than on actual experience, as the number of cases of sarcoma of the breast in any series is too small to give many definite instances of sarcoma directly following an injury to the breast. The more nearly correct statement would be that a larger percentage of cases of sarcoma, but a larger absolute number of cases of carcinoma of the breast, gave a history of injury which was probably the cause of the development of the growth.

Löwenstein, in a series of 9 cases, recorded 5 carcinomata and 4 sarcomata of the breast following injury.

Sex.—Sarcoma of the breast is much more frequent in females than in males. Among the cases reported in the Middlesex Hospital there was only one male in a total of forty-three cases of primary sarcoma of the breast.

Location.—The growth may appear in any part of the breast. In twenty-six cases in which the location of the disease was definitely stated, as reported by Campeche and Lazarus-Barlow, the disease was more frequent in the upper than the lower half of the breast.

Pathology.—Hertzler states that all varieties of sarcoma have been found in the breast, but that the simple or mixed celled is the most common. Various secondary changes may occur in the growth.

Symptoms.—Sarcoma of the breast is usually a rapidly growing tumor and reaches a large size. The tumor is usually softer than a carcinoma and does not show the same tendencies to contraction of the skin or retraction of the nipple. Ulceration of the growth is a less frequent occurrence than with carcinoma. Hemorrhage is a frequent complication of the ulceration. Pain is a late symptom.

Prognosis.—The average duration of life after the beginning of a sarcoma is probably between two and three years.

Treatment.—The treatment of a sarcoma of the breast is the same as for a carcinoma. If the case is operable the same radical operation, that is, the removal of the pectoral muscles and the axillary contents together with the breast, should be performed.

For the inoperable case the indications are the same as for carcinoma.

End Results.—It is not possible to give any reliable statements in regard to the percentage of permanent cures, as the number of recorded cases is limited.

LITERATURE.

Campeche and Lazarus-Barlow. Middlesex Hospital Reports.
Judd. Collected Papers, Mayo Clinic, 1913.
Judd and Sistrunk. Surgery, Gynecology, and Obstetrics, vol. xviii.
Leaf. Cancer of the Breast.
Löwenstein. Ueber Unfallen und Krebs Krankheit.
Mandry. Beitr. z. klin. Chir., Bd. viii, S. 589.
Rodman. Diseases of the Breast.
Warren. Surgical Pathology.
Williams. Diseases of the Breast.
Williams. Natural History of Cancer.

CHAPTER VI.

CARCINOMA OF THE UTERUS.

Etiology.—*Incidence.*—With the possible exception of the stomach, carcinoma occurs in women more frequently in the uterus than in any other organ. It is not possible to state how much greater this frequency is, because there is with carcinoma of the uterus a difference among hospital, autopsy, and mortality statistics. There is also a difference between statistics of the present time and those of a few years ago. The uterus is an accessible organ, and most cases of cancer originating in it are diagnosed clinically and are correctly recorded in hospital and mortality statistics. The stomach is an inaccessible organ, and many cases of gastric cancer are not diagnosed and are incorrectly recorded in statistics. The percentage of recorded deaths from gastric cancer is increasing and may equal that of carcinoma of the uterus.

In a study by Williams of 15,264 deaths of females, from cancer, reported in the Sixty-first Annual Report of the Registrar-General of England and Wales, the largest number, 23.5 per cent., were carcinoma of the uterus. The second largest number, 15.8 per cent., were of cancer of the breast. Cancer of the stomach was in fourth place, with 13.2 per cent. of cases.

In the United States registration area for 1912, constituting about 63 per cent. of the population, there were 7089 deaths from cancer of the "female generative organs." This group included cancer of the uterus and probably of the ovary, Fallopian tube, and the vagina. At the same rate there were in the United States about 11,250 deaths from cancer of these organs during the

year 1912. This was about 25 per cent. of the total female cancer deaths for the year. If malignant growths of the ovaries, Fallopian tubes, and vaginæ, which are relatively infrequent, were excluded it is probable that the percentage would about equal Bashford's statistics. It is probable, therefore, that cancer of the uterus is the cause of about one-quarter of the cancer deaths of females.

Age.—Carcinoma of the cervix uteri occurs at an earlier age than carcinoma of the fundus uteri. Carcinoma of the cervix uteri occurs most frequently between the ages of forty-one and fifty years, of the fundus uteri between fifty-one and sixty years. This is illustrated from the following table adapted from Knack:

	Carcinoma of the cervix uteri.		Fundus uteri.	
Years.	Cases.	Per cent.	Cases.	Per cent.
26 to 30 . . .	16	4.0	1	1.5
31 to 40 . . .	80	20.2	1	1.5
41 to 50 . . .	143	36.2	19	28.8
51 to 60 . . .	115	29.0	33	50.0
61 to 70 . . .	38	9.6	10	15.2
71 to 74 . . .	4	1.0	2	3.0
	396	100.0	66	100.0

This table fairly represents the frequency of carcinoma of the cervix uteri and of the fundus uteri. It does not, however, give the extremes. In the 396 cases of carcinoma of the cervix there was no case under twenty-six years of age. The disease does occur at an earlier age though only rarely. Cragin reported one case of carcinoma of the cervix uteri in a girl under twenty years of age, and there are other cases in the literature. The oldest patient in the series was seventy-four years, but carcinoma of the uterus occurs at later years.

Pregnancy.—It is not easy to determine the influence of pregnancies as a predisposing or an exciting factor in the development of cancer of the uterus. It is not possible to know the number of illegitimate births there have been in any series of cases of carcinoma of the uterus. Neither is it possible to know the number of

such births in general so that the average number of births can be determined for comparison. There are, however, certain facts which, though not absolutely proved, are probably correct. They are not the same for carcinoma of the cervix and of the fundus uteri.

Virgins.—Carcinoma of the cervix uteri is exceedingly rare in virgins, though it does occur. In a series of cases of carcinoma of the cervix uteri reported by Knack, there was no such case, and many clinicians of wide experience have never seen one. Carcinoma of the fundus uteri is more common in virgins than carcinoma of the cervix uteri.

Nullipara.—Carcinoma of the cervix uteri is more common in nulliparæ than in virgins. The probable explanation is the greater frequency of inflammation of the cervical canal and erosions of the cervix among married women even though they have had no children. Of the married women in Knack's series of cervical carcinoma, 5.9 per cent. had never been pregnant. In Germany, as reported by Knack, 11.2 per cent. of marriages are childless; that is, there is a smaller percentage of sterile women among the cancer cases than in the general population. There is a smaller percentage of cases of carcinoma of the cervix uteri among women who have never been pregnant than among all married women of the general population. The difference is not great and there are two factors which would partly explain it. The age of the cancer cases was probably greater than that of the general population. The histories of the cancer cases, especially in regard to early pregnancies, abortions, etc., were probably more accurate than such records in regard to the general population, and more women who were not nulliparæ would be counted as such from the general population than among the cancer cases whose histories were taken by physicians in whom they had confidence. It is difficult to conceive of anything about cancer of the cervix or the possible influences that cause it that would increase the chance of pregnancy;

that is, that would diminish the number of nulliparæ as the figures themselves would indicate. It must be accepted, therefore, that next to virgins, women who have never been pregnant are least likely to develop carcinoma of the cervix uteri.

The number of nulliparæ among the cases of carcinoma of the fundus uteri is in distinct contrast to the number among the cases of carcinoma of the cervix uteri. Instead of being less than normal, as in the case of the latter, there are more than the normal number of women who have had no children among the cases of carcinoma of the fundus uteri. Of Knack's series, 18.8 per cent. of all the cases and 13.3 per cent. of the married women were childless. The average percentages of 14 observers quoted by him was 25.6 per cent. Some of the percentages quoted were based on a small number of cases and were therefore subject to wide varition. The smallest percentage was 3.3 per cent. and the highest 56.3 per cent. Of 19 cases reported by Cullen, 10 cases, or 52 per cent., had never been pregnant.

It must not be interpreted from the figures given that the chances of a woman having a carcinoma of the fundus uteri are diminished if she bears children. The probable explanation is that the conditions (whatever they may be) that influence the production of a carcinoma of the fundus uteri are also influential in causing the sterility.

Uniparæ, Multiparæ.—Of 364 cases of carcinoma of the uterus (including both the cervix and the body of the uterus) in married women as reported by Knack, there were an average of 5.6 full-term births for each woman compared with 4.15 to 4.3 such births for the married women of Germany.

Of the cases in Knack's series of carcinoma of the cervix uteri, 11.2 per cent. had only one child and 82.3 per cent. more than one. Of the cases of carcinoma of the fundus uteri, 22.3 per cent. had one child and 61.1 per cent. more than one. The percentage of married women who have more than one child, according to figures quoted by

Knack, is between that for carcinoma of the cervix uteri and that of carcinoma of the fundus uteri and is probably about 76 per cent. This would indicate that cases of carcinoma of the cervix uteri have a larger number of children; in other words, an increase in the number of children increases the cases of carcinoma of the cervix uteri. This is not shown for carcinoma of the fundus uteri. The percentage of cases of carcinoma of the fundus uteri that have more than one child is considerably less than normal. There is in this the suggestion that some influence, possibly the result of the one pregnancy, produces both the sterility and the malignant growth of the fundus uteri.

The following table from Theilhaber shows plainly the relationship between the number of births and the frequency of carcinoma of the cervix and of the fundus uteri:

Number of births.	Carcinoma of cervix.	Per cent.	Number of births.	Carcinoma of fundus.	Per cent.
0	9	2.9	0	11	27.5
1	25	8.1	1	4	10.0
2	29	9.4	2	9	22.5
3	36	11.7	3	5	12.5
4	23	7.4	4	2	5.0
5	34	11.0	5	2	5.0
6	40	13.0	6	3	7.5
7	111	36.1	7	4	10.0
	307	99.6		40	100.0

This table indicates that as the number of births increase, there is in general an increase in the percentage of occurrence of carcinoma of the cervix uteri, but that the reverse is true for carcinoma of the fundus uteri. The largest number of the cases (27.5 per cent.) of carcinoma of the fundus uteri were nulliparæ, and, in general, the percentage decreased as the number of births increased. The average number of children for each case of carcinoma of the cervix uteri was 4.8, and for each case of carcinoma of the fundus uteri 2.5. Theilhaber found that the average number of children for women not suffering from cancer,

but who had passed the child-bearing age, was between three and four. The number of children in the cases of carcinoma of the cervix uteri was above the average, but in those of carcinoma of the fundus uteri below average. Theilhaber found among women over forty-five years of age not suffering from cancer, 19.8 per cent. of sterility; among the cases of carcinoma of the uterus of corresponding ages, scarcely 4 per cent. of sterility. He also reported an interesting observation in regard to the relation between the average age at which carcinoma of the cervix uteri occurred in relation to the number of births. The average age at which carcinoma of the cervix uteri occurred in sterile women was fifty-seven years, in women with one child, fifty-one years, and in women with six children forty years.

Abortion and Miscarriages.—It is difficult to show by statistics the relationship between cancer of the uterus and abortions and miscarriages. Even in countries and cities in which they must be legally registered the reports are, for obvious reasons, far from accurate. The most reliable statistics are from hospital records, as they are made by physicians in whom confidence is placed by the patient. These records are reasonably accurate for these cases, but they are records of patients, that is, of women who are ill and not of women in general. It is variously estimated that there is one abortion to every four to twenty full-term births. Knack, taking as an average for women in general one abortion in ten births, found abortions relatively more frequent than the average both for carcinoma of the cervix uteri and of the fundus uteri. His statistics show for carcinoma of the cervix uteri one abortion to every 8.5 births, which is slightly more frequent than the average, and for carcinoma of the fundus uteri, one to every 3.5 births. The greater relative frequency of abortions in cases of carcinoma of the fundus uteri is striking, and suggests that there may be in the uterus a condition that produces the abortion which may also be a factor in the development of the

carcinoma. Theoretically, the action of abortions on the development of carcinoma of the uterus is probably the same as that of full-term pregnancies. With an abortion or miscarriage, the cervix may be injured even more than by a delivery at full term, when the cervix is more softened and dilates more readily. Naturally an injury or erosion which may be a factor in the development of a cancer would have the same influence whether the result of an abortion or a full-term delivery.

Obstetric Operations.—There are no statistics available to prove the influence of the various obstetric operations, such as turning, the use of forceps, bags, cervical dilators, etc., on the production of uterine cancer, and it is hoped that in the future there will be more careful records of these procedures.

Theoretically, as obstetric operations produce injuries and resulting inflammations, they may influence the development of uterine cancer.

The influence of these agencies—pregnancies, abortions, and obstetric operations—is exerted by producing conditions which are the probable factors in the development of carcinoma of the cervix uteri. They are (1) lacerations, (2) erosions, and (3) cervical inflammation. These conditions cannot be separated; one is dependent upon the other; and it is not possible to state how or to what extent these conditions influence the development of a carcinoma of the cervix uteri. It is merely known, as has been shown, that carcinoma of the cervix is of more frequent occurrence the greater the number of pregnancies and that lacerations and erosions of the cervix uteri are the result of such pregnancies. It is also believed that injury, especially repeated injuries and chronic irritations, cause cancer, and therefore it is a fair assumption that the repeated pregnancies predispose to cancer of the cervix uteri by causing the lacerations, erosions, and cervical inflammations.

Lacerations.—Lacerations of the cervix uteri are usually on one or both sides of the cervix. Carcinoma rarely

begins on the side, but usually on the anterior or posterior lip. This is used as an argument against a laceration of the cervix uteri being a factor in the production of a carcinoma, and in reply it has been stated that in the anterior and posterior lips there are microscopic injuries, and in these microscopic injuries the cancer develops. This is probably not the way in which a laceration of the cervix uteri influences the development of a cancer.

A cancer rarely develops in a healthy healed scar. Abdominal scars as the result of operations are numerous, but a cancer in such scars is practically unknown. At the orifice of the vagina from the rupture of the hymen and from injuries at confinements scars are very frequent, but carcinoma is equally rare. These injuries, however, are healed, and in such healed healthy scars carcinoma rarely occurs. Some lacerations of the cervix uteri which are produced at childbirth completely heal, though the evidence of the lesion is still present; that is, the laceration has been entirely covered over by the flat epithelium of the cervix. In such cases the external os is of normal size, there is no eversion of the cervical mucous membrane and no erosions. Such a case is probably little or no more likely to develop carcinoma of the cervix uteri than if no laceration had ever existed. In other cases the laceration divides the cervix into an anterior and a posterior lip, the cervical mucous membrane is everted, and erosions are formed.

Lesions composed of the everted cervical mucous membrane, the so-called erosions, which heal slowly and may exist for a long period of time, are formed in this way. It is in the long existing, unhealed lesion that carcinoma is theoretically most likely to develop. These erosions, the result of a laceration, are mostly on the anterior and posterior lips. At the sides, at the angle of the laceration, where there is the greatest amount of scar tissue and where carcinoma is least likely to develop there are fewer or no erosions, and the flat epithelium of the vaginal portion of the cervix covers over the angle

of the laceration nearly to the epithelium of the cervical canal.

The most probable explanation of the greater frequency of carcinoma of the cervix uteri in the anterior or posterior lip of the cervix, than at the sides in the laceration, is the more frequent occurrence of erosions in the former places, and that unhealed erosions predispose to carcinoma more than scar tissue. In other words, a laceration of the cervix uteri predisposes to the formation of a carcinoma not on account of the scar tissue, but of the erosions which are formed. If this were not the case, there would be nothing gained in the prevention of carcinoma of the cervix by repairing lacerations. The repair of a laceration of the cervix cures the erosion, but scar issue will still remain as there is some cicatricial tissue as the result of the repair.

Erosions.—These may result from lacerations of the cervix, as has been described, or from cervical inflammation and possibly from displacements of the uterus. It is not possible to state positively that carcinoma of the cervix ever starts as the result of an erosion. Many observers state that they have never seen such a case. Certainly, there are many cases of erosions of the cervix that have remained benign for years.

By analogy with similar conditions in other parts of the body, it is fair to assume, however, that a carcinoma of the cervix uteri may be caused by a cervical erosion. An erosion is a lesion which is slow to heal, located at the junction of flat and cuboidal epithelium, and exposed to irritation. These are conditions generally believed to predispose to the development of cancer. Nothing more definite can be stated in regard to the relation between an erosion of the cervix and carcinoma.

Cervical Inflammation.—The influence of cervical inflammation in the causation of carcinoma of the cervix is both direct and indirect.

It is generally believed that a chronic inflammation produces changes in the tissues that predispose to the

formation of a malignant growth. Theilhaber strongly holds this belief. If this is true in other parts of the body it is probably also true in the cervix.

The causation of carcinoma of the fundus uteri is less apparent than that of the cervix uteri. There are no apparent lesions, such as lacerations or erosions in the fundus uteri, that seem to have any influence in the formation of a carcinoma. It has been shown that carcinoma of the fundus uteri is especially frequent in women who are sterile or who have had only one child, and that the average number of children in women who have carcinoma of the fundus uteri is less than usual. It is hardly possible that sterility itself in any way would increase the chances of the development of a malignant growth in the uterus. It is more natural to seek for a cause which might be responsible for the sterility and also for the carcinoma. A uterine polyp is probably such a lesion. Cases are recorded in which the carcinoma of the fundus uteri apparently started in a polyp. Such growths in other parts of the body are believed to predispose to the formation of carcinoma and might likewise do so in the uterus. Such a lesion could cause the sterility. It is possible that a narrow cervical canal, or a sharp angle of flexion, by retaining menstrual discharge, might predispose to the formation of cancer as well as cause sterility. It is possible that a chronic endometritis might be a predisposing cause.

Pathology.—*Carcinoma of the Cervix Uteri.*—Histologically there are two types of carcinoma of the cervix uteri, namely, the squamous-celled and the columnar-celled. The former usually begins in the flat epithelium of the vaginal portion of the cervix, especially at its junction with the cervical canal. The latter ordinarily starts from the columnar cells of the cervical canal or the glands leading to it. Clinically it is usually impossible to distinguish the histological varieties.

Hertzler, for the sake of greater clearness of description, divides carcinoma of the cervix into three stages:

(1) where the disease is limited to the cervix; (2) where the growth has extended to the parametrium, but the uterus is still movable, and (3) where the disease has extended to the parametrium and possibly also involved one of the neighboring organs and fixed the uterus. One stage, of course, merges directly into the next, but this division is convenient for descriptive and also for clinical purposes.

First Stage.—There is an early stage when the carcinoma is a small nodule or diffuse infiltration of the cervix. This stage, however, is rarely seen clinically, but is discovered microscopically in a cervix removed for other reasons. The earliest stage ordinarily seen clinically is the formation of small elevations or projections from the cervix, which on account of its appearance is often described as a cauliflower growth. This cauliflower mass by rapid growth may reach a considerable size with a relatively small attachment to the cervix—a polypoid growth. Usually as this mass increases in size, its attachment to the cervix also increases, and ultimately involves the whole of the cervix. At some stage this mass breaks down and forms an ulceration. In some cases the ulceration forms early, so that at no time is a cauliflower growth seen. Most frequently the two processes are present together. Around the edges there is an abundant cauliflower growth with sloughing and ulceration in the centre. These are the two clinical varieties, the polypoid or cauliflower growth and the ulcerative. They are both a part of the same process, the ulceration being a later stage than the cauliflower growth. Cases that are seen in the first stage are favorable for operation, and the outlook for a permanent cure is favorable.

Second Stage.—In this stage the growth extends outside of the cervix and involves the cellular tissue of the parametrium, but not to an extent to make the uterus immovable. This involvement is partly by direct extension and partly through the lymphatic system. The extension

of the growth is mostly to the sides, in the cellular tissue of the broad ligaments, and more rarely toward the bladder or rectum. There may also be extension upward into the fundus uteri or downward onto the vaginal walls. This extension into the uterus or onto the vaginal wall does not limit the mobility of the uterus nor influence the operability of the case as much as the lateral extension into the cellular tissue of the broad ligaments. The extension outside of the uterus does not usually occur until the cervix is partly destroyed by the ulcerative process of the first stage of the disease, and as a result of this septic process, a part of the induration around the uterus may be of an inflammatory character. Cases in the second stage are usually operable, but the outcome is distinctly less favorable than in those in which the growth is limited to the cervix uteri.

Third Stage.—In this stage, the lateral progress of the growth has usually extended into one or both broad ligaments and fixed the uterus in the pelvis. The normal mobility of the uterus is no longer present. The extension of the growth to the front and to the back is present but less marked than that to the sides. The growth may extend from the cervix uteri on to the anterior or posterior vaginal wall, and through the rectal or bladder wall as shown by proctoscopic or cystoscopic examination; but it is the exceptional case, even in the terminal stage, in which there is an ulceration into either of these organs forming a vesicovaginal or a rectovaginal fistula.

The ureter is directly involved in the disease only in the late stage. Even though the growth has extended into the pelvic cellular tissue and entirely surrounded it, the wall of the ureter may not be involved. More frequently, on account of the pressure of the growth, there is an obstruction of the ureter producing a hydro-ureter. As a result of this same obstruction a distention of the pelvis of the kidney may occur and a hydronephrosis may be produced. By infection a more advanced stage of the same process may be reached and the hydronephrosis

converted into a pyonephrosis. Changes in the ureter and the kidney are among the most frequent terminal complications of carcinoma of the cervix uteri.

By obstruction to the uterine canal, there may be interference with proper drainage of the fundus and a pyometrium produced. This is not usually of large size, as the obstruction is due to surfaces of the growth coming in contact and not to an organized stricture, and pressure of the accumulated discharge or sloughing of the growth overcomes it.

In the end, as a result of the extension of the disease, the pelvis is filled with the malignant growth and the uterus is fixed on all sides. On vaginal examination, in addition to the ulcerated cervix uteri, the parts are found to be hard, rigid, and indurated, and not soft and pliable as under normal conditions.

These cases are practically all inoperable. Any case of carcinoma of the cervix uteri, with the uterus fixed by the extension of the malignant growth, is beyond the reach of permanent benefit from present surgical technique. Palliative operations, as described elsewhere, may be indicated to control the symptoms.

Metastases.—These occur late both in the lymphatic glands and in the distant organs. This fact adds greatly to the success of the operation for carcinoma of the cervix uteri.

The lymphatic glands that are first involved are the one located at the crossing of the uterine artery and the ureter and those along the iliac vessels. More rarely a gland in the sacro-iliac ligament, the superficial and deep inguinal glands, and those higher in the abdominal cavity are involved. Enlarged glands are not necessarily carcinomatous. They may be enlarged as a result of the septic condition of the cervix or from some entirely separate process, such as a tuberculous infection. Involvement of lymphatic glands indicates a bad prognosis as to a permanent cure. Wertheim, Sampson and others, however, have reported cases of carcinoma of the cervix

uteri in which carcinomatous glands have been removed and the case remain well beyond the five-year period.

Metastases in distant organs occur more frequently and at a later period than in the lymph nodes.

The vagina may be involved by direct extension, and in most cases in which the growth has extended beyond the cervix uteri it has encroached on the vaginal wall at some point. More rarely the vaginal wall may be involved by direct contact with the cervical growth. In such cases a malignant ulcer is present in the vaginal wall entirely separated by normal tissue from the primary growth. It has been doubted that a contact cancer in the vagina can result from a carcinoma of the cervix uteri, and these cases are explained by retrograde metastases. It is not probable that cancer cells, under the septic conditions existing in the vicinity of a cervical carcinoma, can be engrafted on normal vaginal mucous membrane. If, however, a benign ulceration is first produced by the irritation of the growth it is more probable that cancer cells might become engrafted on it and the contact cancer be developed. A secondary growth in the vagina does not usually interfere with the operability of the case.

The fundus of the uterus may be involved secondarily from a carcinoma of the cervix uteri. By direct extension the cervical growth may extend along the uterine mucous membrane and involve the whole or the greater part of the uterine cavity.

In other cases the growth in the fundus may be separated from that of the cervix by an area that is apparently normal. The most probable explanation of this condition is that the growth in the fundus occurs by metastases from that of the cervix through the lymphatic vessels. Cullen has shown that there may be numerous microscopic growths secondary to a cervical carcinoma in a uterine fundus that microscopically seems normal. These growths may be on the mucous membrane or deeper in the uterine structure.

Carcinoma of the Fundus Uteri.—In the earliest stage adenocarcinoma of the body of the uterus is a limited circumscribed growth and may begin at any point in the cavity of the uterus. This tumor, as it increases in size, may remain localized or it may quickly spread, forming a diffuse growth. There may be, therefore, in the body of the uterus at an early stage a localized or diffuse adenocarcinoma. In the earliest stage the character of the mucous membrane is so little changed that it can be distinguished from the normal only by microscopic examination. Later it becomes thickened and elevated with the formation of delicate processes or outgrowths. The formation of these processes takes place toward the cavity of the uterus, and also toward the deeper structures. In some cases the tumor grows largely toward the cavity of the uterus, filling it with the malignant growth, and in other cases it extends more toward the deeper tissues of the uterus. This may be due to special characteristics of the individual growth or to special resistance of the uterus. In the late stage these differences are not noticed, and not only is the cavity filled with the malignant growth, but the wall of the uterus is also entirely infiltrated with it.

The malignant tissue is soft and friable and easily breaks down. The malignant infiltration of the uterine walls makes it much softer than normal. Clinically this may be detected by a bimanual examination or with the curette. These cases should not be curetted excepting when necessary to make a diagnosis, on account of the danger of cancer cells entering the normal tissues. Not infrequently there is no other way to make a correct diagnosis. In curetting an advanced case of carcinoma of the fundus uteri, a larger amount of tissue is removed than in an ordinary case of endometritis. Ordinarily in curetting after a part of the endometrium has been removed the uterus feels firm to the curette, but it is not so with a carcinoma of the body of the uterus that has passed the earliest stages. In such a case the uterine

wall has become softened to such an extent that it is easily removed in pieces with a curette. In an extreme case the uterus is converted into a shell of muscular tissue and peritoneum enclosing a malignant growth. Special care must be taken to cease curetting as soon as the diagnosis is made or suspected.

Extension.—When the growth reaches the peritoneum, elevations will appear on the surface of the uterus. At first these are small and separate, but later they grow together and may change the contour of the uterus. At first these elevations of malignant tissue are covered with peritoneum. Later it breaks through the peritoneum and may form adhesions to the intestines and omentum, which may become secondarily involved, or it may cause general peritoneal carcinomatosis.

Extension to the pelvic connective tissue, for anatomical reasons, occurs later than in carcinoma of the cervix uteri. When a carcinoma of the cervix uteri reaches the outside of the uterus it comes directly to the connective tissue at the bases of the broad ligaments. A carcinoma of the fundus uteri when it reaches the surface comes to the peritoneum except at the sides where it is supported by the broad ligaments.

As a tumor in the fundus uteri may be secondary to the cervical carcinoma, so also are reported tumors in the cervix and vagina secondary to a growth in the fundus uteri. One explanation of the formation of these secondary growths is that there has been a back flow in the lymphatic vessels and the cancer cells have been carried with it. Another explanation that has been made is that the pieces of cancerous tissue from the primary growth have become implanted on the mucous membrane of the cervix or on the vaginal wall. In support of the latter explanation of the occurrence of these secondary growths is their location most frequently on the posterior vaginal wall where, theoretically, they would be most likely to occur. The formation of a secondary growth in this manner and under such circumstances would be very

unusual if it ever occurred. A third possibility is that the cervical carcinoma was the primary growth and that in the fundus was a metastasis.

Symptoms.—For greater clearness of description the symptoms of carcinoma of the cervix and fundus uteri will be given separately.

Carcinoma of the Cervix Uteri.—The symptoms, as was done with the pathology, will be described for three stages, though the division is artificial and symptomatically as well as pathologically no such division exists.

First Stage.—Subjective Symptoms.—There are cases of carcinoma of the cervix uteri that give no subjective symptoms during the first stage. Theoretically this seems hardly possible, but clinically there is occasionally a case in which the growth has extended beyond the cervix before there were any symptoms that were noticed by the patient. There are two symptoms which are in practically all cases the first subjective symptoms of carcinoma of the cervix uteri. They are: (1) change in the mestruation or bleeding from the vagina, and (2) change in the vaginal discharge. Irregular bleeding and a change in the vaginal discharge are symptoms which should always raise the suspicion of a malignant uterine growth. They are usually the only subjective symptoms at the time the patient first seeks advice.

1. *Bleeding.*—This symptom is of special significance when it occurs after the menopause. When there is a return of blood or a bloody discharge after the menstruation has ceased, a uterine cancer is the most frequent cause. Frequently the first indication is bleeding following intercourse, a vaginal douche, or any other traumatism. The reason for this is obvious. The growth is mechanically injured and the bleeding is the result of the trauma. The bleeding may first be noticed after straining to move the bowels. In such cases the patient may be deceived in regard to the source of the bleeding and think that it is due to hemorrhoids. The amount of bleeding may be a "spotting" or slight staining between the regular menstrual

periods, or rarely, however, in the early stage enough to endanger the life of the patient. In other cases, especially in carcinoma of the scirrhus type, there may be no bleeding at all.

2. *Change in the Vaginal Discharge.*—Most women have a slight vaginal discharge, which should not be considered abnormal. Some women have considerable discharge, and if it has existed for some years it is doubtless due to some other cause than carcinoma of the cervix uteri. If, however, a woman who has had no discharge begins to have one, or if the discharge which has existed for some time changes in character or amount, there should be a suspicion of carcinoma of the cervix uteri. In this first stage, it is the change in the character or in the amount of the discharge which is the suspicious symptom, more than the discharge itself. The discharge is usually thin and watery, more or less discolored with blood, and of a characteristic odor.

3. *Pain.*—This symptom is usually absent during this early stage. If present, it is probably due to inflammatory conditions about the uterus or to other pelvic lesions and not to the cervical cancer.

4. *General Health.*—This is not changed. There is loss of neither flesh nor strength.

First Stage, Physical Signs.—The cervix may show an erosion or contain a nodule the nature of which is discovered only by microscopic examination. These very early cases are rarely seen. Usually there is a cauliflower growth or an ulceration in the cervix. The characteristic feeling, which is one of dense hardness, is of greater diagnostic value than the appearance of the ulceration and is usually sufficient to establish the diagnosis. The statement that "the doubtful case is rarely malignant" is true.

In this stage there are no objective signs other than those of the cervix just described. The uterus is not changed materially in size, position, or mobility.

It is possible to give only an indefinite estimate of the

duration of the first stage. It is usually under four months from the beginning of the first symptoms.

Second Stage, Subjective Symptoms.—1. *Bleeding.*—Though it may be absent, bleeding is more constant than it is in the first stage, and retains the same general characteristics, such as "spotting" between regular menstruations, increased in amount by intercourse, injury, etc. Profuse bleeding resulting from ulceration of an artery or from a digital examination is a more frequent occurrence than in the earlier stage.

2. *Discharge.*—This is usually at this period a characteristic symptom. The discharge is thin and watery and has an odor which is peculiar to the disease. Frequent douches will not entirely control the discharge or the odor.

3. *Urinary Symptoms.*—Extension of the cervical carcinoma to the anterior vaginal wall and to the bladder may occur during this stage. Increase in frequency and painful urination are frequent symptoms. These symptoms do not necessarily mean that the bladder wall itself is involved by the growth. It may be the result of an inflammatory reaction in the bladder from the ulcerated cervix. The bladder often may be separated successfully from the anterior vaginal wall even if the latter is involved by the malignant growth.

4. *Rectal Symptoms.*—These are ordinarily absent during this stage. Anatomically, the rectum is less closely related to the cervix uteri than the bladder. The growth may have extended on to the posterior vaginal wall and still be separated from the rectum by the cul-de-sac of Douglas.

5. *Pain.*—This symptom is usually present during this stage. It may be due to the involvement or pressure on the nerves by the growth or to the inflammation of the tissues about the uterus. The pain may be referred to the back, to the lower abdomen on either or both sides, or down either or both legs.

6. *General Health.*—There is a beginning loss of flesh and strength, and the patient shows the early general

signs of a malignant growth. It is not possible to give the period of time of this second stage in a definite way. Roughly, it occurs from the fourth to the eighth month from the first symptoms. Rarely is a case that has lasted over eight months operable.

Second Stage, Physical Signs.—The cervix is largely destroyed by an ulceration. The vaginal wall, especially to the front of the cervix, may also be ulcerated. On one or both sides of the cervix there is an infiltration of the broad ligaments. The mobility of the uterus may be decreased. There is usually no material change in the size of the uterus.

Third Stage, Subjective Symptoms.—(1) Bleeding and (2) discharge are the same as during the second stage. Pain on account of the extension of the disease is a more constant symptom and is more severe. Pain is distinctly increased if the peritoneum becomes involved.

3. *Rectal Symptoms.*—There may be increasing constipation. This may be caused by definite obstruction due to the rectal involvement by the growth, or it may be due to the pain produced by the passage of feces over the growth. If a rectovaginal fistula is formed, the feces may be passed through the vagina.

4. *Urinary Symptoms.*—There may be pain and increased frequency of urination. The urine may contain pus, blood, and mucus, indicating that the growth has involved the bladder wall. The urine may flow into the vagina if a vesicovaginal fistula is formed. The symptoms of pyelitis, hydronephrosis and pyonephrosis may be present.

5. *General Condition.*—There is the general loss of flesh and strength common to the terminal stages of all malignant growths. Metastases may form in the liver, lungs, or kidneys, but usually only during the latest stages of the disease. There may be a general septic infection due to absorption from the ulcerated cervix. The loss of blood may produce a profound secondary anemia.

Third Stage, Objective Signs.—The uterus is not increased materially in size, but it is firmly fixed in the

pelvis. The cervix uteri may be entirely destroyed by the ulceration and the examining finger may pass into the cavity of the uterus without meeting any obstruction. There is a deep excavation lined with irregular necrotic tissue. The vagina may be ulcerated only at the upper part or the malignant infiltration may extend down as far as the vulva. It may communicate directly by a fistula with the bladder or the rectum. On either side of the uterus the malignant infiltration of the broad ligaments can be felt. The bladder may, by cystoscopic examination, be found to contain a malignant growth or ulceration. Similar involvement of the rectum may be discovered by proctoscopic or digital examination. The inguinal glands may be found enlarged.

Carcinoma of the Fundus Uteri.—*Subjective Symptoms.*—The two first symptoms of carcinoma of the fundus uteri are the same as those of the cervix uteri. They are: (1) irregular bleeding and (2) change in the vaginal discharge.

1. *Bleeding.*—This may be absent until the disease is well advanced. If the patient is still menstruating, there may be only an increase in the duration, amount or frequency of the menstruation. The most frequent history is that after a period of some years of absence of menstruation (carcinoma of the fundus uteri is most frequent at an advanced age) there is a return of bleeding which is irregular in amount and in time.

There are cases which are undoubtedly carcinomata of the fundus uteri which give a history of bleeding extending back over a period of years. It is incorrect to assume that the malignant growth has always existed as long as the irregular bleeding. The irregular bleeding may have been due to an endometritis, a fibroma uteri, a uterine polyp or some other cause and the malignant growth a subsequent development. The bleeding of carcinoma of the fundus uteri is not influenced by trauma to the same extent as cervical carcinoma.

2. *Change in the Vaginal Discharge.*—This symptom is more constant and is usually earlier than the irregular bleeding. The discharge is usually thin and watery. In the early stages, the odor of the discharge is not enough to be noticed by the patient or on the examining fingers, but at a later stage it is more marked. The discharge may contain pieces of malignant tissue but only at an advanced stage of the disease at which other symptoms easily establish the diagnosis.

3. *Pain.*—As in cancer elsewhere this is not an early symptom of carcinoma of the fundus uteri, and may not be a marked symptom at any stage of the disease. There is probably less pain on an average with carcinoma of the fundus uteri than with most cancer. The explanation of this is twofold. The uterus relatively is an insensitive organ, and is well protected from outside injury, and a growth in it may reach considerable size without involving any sensitive part.

With the exception of menstruation and child-bearing the uterus has no special function, and on account of the age of the patient and the nature of the disease both of these functions may have ceased. In the stomach the intestines, the rectum, the tongue, etc., a carcinoma is constantly irritated and injured by the movements and use of the organs. It is different with a carcinoma of the fundus uteri, an organ which is quiescent and protected from injury.

At an advanced stage there may be paroxysms of pain as though the uterus were attempting to expel a foreign body from the cavity. Such pain is usually relieved by a curettage. A curettage is, however, not ordinarily performed for carcinoma of the fundus uteri excepting for diagnostic purposes.

When the growth has extended through the wall of the uterus and involved the peritoneum there is usually considerable abdominal pain, but even when the peritoneum is involved the pain may not be severe. If the uterus is

increased in size there may be a sense of pressure and falling from its weight.

4. *Urinary Symptoms.*—These are not present in the early stages, but later there may be symptoms of vesical irritation. This may be the result of pressure or the dragging of the heavy uterus or of the involvement of the bladder by the growth.

5. *General Condition.*—Carcinoma of the fundus uteri does not involve an organ whose function is to support the nutrition or general vitality of the organism. The bleeding from it does not cause the secondary blood changes as early as does carcinoma of the cervix uteri. Metastases occur only late in the disease. Frequently the disease has reached the inoperable stage before the general health is affected with more than a moderate secondary anemia.

Objective Signs.—The one sign of importance is the size of the uterus. It must be remembered that most cases of carcinoma of the fundus uteri occur in women well passed the menopause and that the uterus in such cases is atrophic and under normal size, that is, it is a senile uterus. When a carcinoma of the fundus uteri has advanced sufficiently to give any subjective symptoms, that is, either bleeding or discharge, the uterus is nearly always of at least normal size—it is larger than a senile uterus. Reversely, an atrophic uterus, the small senile uterus, is rarely the seat of a malignant growth.

As the disease advances the uterus increases in size. It rarely reaches a size which is larger than the uterus of a two or three months' pregnancy.

The consistency in the early stages is that of a normal uterus. Later the uterus is soft and flabby. The cervix is usually not changed; it may be open. This is the condition if the tumor grows through the cervical canal or the uterus attempts to expel it.

Diagnosis.—There are three conditions from which a carcinoma of the fundus uteri must be distinguished:

1. A *submucous fibroma uteri,* if of small size so that the uterus is only moderately and symmetrically increased in size, may closely simulate a carcinoma of the fundus uteri. A curettage usually is necessary to establish the diagnosis. The discovery of the fibroma in the uterus and the microscopic examination of the tissue removed will decide the diagnosis.

2. *Endometritis.*—At the menopause an endometritis causing irregular bleeding and a vaginal discharge is a frequent occurrence. A curettage and a microscopic examination of the tissue removed is the only way to disinguish between an endometritis and an early carcinoma of the fundus uteri. This should be done under an anesthetic and with an immediate microscopic examination of the tissue removed.

In some of these cases the microscopic examination shows only a benign endometritis, but the irregular bleeding continues. Regardless of the microscopic examination, such cases should be considered suspicious and carefully watched. A second curettage or possibly a hysterectomy may be necessary.

3. *Senile Vaginitis.*—This is a common lesion which gives symptoms closely resembling a carcinoma of the fundus uteri. A small atrophic uterus is against a carcinoma of the fundus. The recognition of the senile vaginitis, and its cure by proper treatment, will definitely establish the diagnosis.

Course.—It is difficult to correctly estimate the average duration of carcinoma of either the cervix or the fundus uteri because it is impossible in most cases to determine the beginning of the disease because of its gradual onset.

In general, carcinoma of the cervix uteri runs a more rapid course than carcinoma of the fundus uteri. The duration of the former on the average is two to two and a half years and of the latter about a year longer. This difference in the duration of the disease in the two places may be due to the anatomical conditions. Carcinoma of the fundus uteri is protected from mechanical

injury, frequent movement, and for a longer time from secondary infection. These conditions probably influence the spread of the disease. The relative duration of the disease in the two places is also influenced by the earlier involvement in carcinoma of the cervix of organs such as the rectum, bladder, and ureters which indirectly may shorten the duration of the disease.

The duration of carcinoma of the cervix uteri may be prolonged by proper treatment, even if the case is inoperable. The cervical discharge and bleeding and the secondary infection may be limited as described elsewhere.

Treatment.—This will be considered under three headings: (1) diagnosis, (2) operable cases, and (3) inoperable cases.

1. DIAGNOSIS.—Carcinoma of the cervix uteri can usually be diagnosed by the appearance and feeling of the cervix. A piece of the growth should not be removed for microscopic examination, excepting in the doubtful cases, because of the danger of scattering cancer cells beyond the uterus. For the same reason, unnecessary or too thorough examination of carcinoma of either the cervix or fundus uteri should be avoided. Any pieces of the cervix uteri which are removed for any purpose should always be subjected to microscopic examination in order to discover the early and unsuspected cases.

Carcinoma of the fundus uteri can usually be diagnosed only by a curettage. It is therefore necessary to curette into malignant tissue to establish this diagnosis regardless of the danger of scattering cancer cells. As soon as the diagnosis is established (as can be done in some cases with the curette without further examination), or sufficient material has been removed for a frozen section for a microscopic examination, no further curetting should be done in order to limit this danger as much as possible. In every case that is curetted, whether carcinoma is suspected or not, the curettings should be examined microscopically in order to discover early and unsuspected cases.

2. Operable Cases.—Under this heading are included the cases of carcinoma uteri which are sufficiently limited, that the uterus can be removed with the expectation of curing or prolonging the life of the patient. Cases that are so far advanced that no operation other than a palliative one, such as cauterization or a curetting for the relief of the symptoms, can be performed are not included. For the clearness of description, though it may require some repetition, carcinoma of the cervix uteri will be considered separately from carcinoma of the fundus uteri.

Carcinoma of the Cervix Uteri.—Of the three stages into which the course of a carcinoma of the cervix uteri was artificially divided for the description of the symptoms, all the cases in the first stage, that is, the stage in which the disease is limited to the cervix uteri are operable. All the cases in the third stage, that is, the stage in which the growth has extended so far that the uterus is fixed in the pelvis are inoperable. Of the cases in the second stage, some are operable and some are not. In general, if the growth has not extended so far that the uterus is fixed, the case is operable. Usually if the growth outside of the uterus has extended not over an inch into the broad ligaments, and only moderately on to the vaginal walls the case would be benefited by the removal of the uterus and should be considered operable. These statements, however, should not be considered absolute, and the general condition of the patient, as well as the local lesion, must be considered. In a patient who is thin but in good general condition—in other words, one on whom the operation would be relatively easy and who would be a favorable operative risk—a more extensive carcinoma of the cervix uteri would be considered operable than in a woman on whom the operation would be associated with greater risk.

A carcinoma of the cervix uteri may be limited in extent and the case operable so far as the local lesion is concerned, but inoperable on account of metastases in other organs or in lymphatic glands. Frequently an exploratory

celiotomy is necessary to determine the operability of the case. Only after the abdomen has been opened and the condition of the liver, intestines, peritoneum, omentum, and lymphatic glands, determined by direct inspection, can the operability of the case be decided. It may be necessary to remove a lymphatic gland for examination of a frozen section to determine the nature of its enlargement.

After the abdomen has been opened, if metastases are found in abdominal organs the case is inoperable and usually the uterus should not be removed. There are, however, some cases with metastases in which the removal of the uterus is indicated. If the general and local conditions of the patient are such that a hysterectomy can be done without special risk it should be done. The removal of the uterus, with the infected sloughing growth in the vagina and the control of the bleeding and foul discharge, will add to the mental and physical comfort of the patient even if her life is not prolonged.

Involvement of the lymphatic glands that are accessible is not a contra-indication to removal of the uterus though it diminishes the chances of a permanent cure.

Carcinoma of the Fundus Uteri.—An exploratory celiotomy is necessary more often for cases of carcinoma of the fundus uteri than of the cervix uteri. If the growth has extended through the wall of the uterus and involved the peritoneum there will probably be multiple peritoneal growths in other parts of the abdomen and adhesions to the viscera, and the case is incurable. As with cases of cervical carcinoma, as the abdomen is already open, if the local and general conditions are such that the uterus can be removed without special risk, a hysterectomy should be performed to cure the discharge and bleeding. This will add greatly to the comfort of the patient and may temporarily improve the general health, but will, of course, not cure the condition.

Carcinoma of the fundus uteri remains operable for a longer time after the first symptoms than carcinoma of the cervix uteri.

Percentage of Operability.—There are no statistics from which any close estimate can be made of the percentage of cases of carcinoma of the cervix uteri which are seen to be still operable. Such a percentage would vary greatly for the same cases with different operators. Some men knowing that the removal of the uterus is practically the patient's only hope will assume a higher operative risk for a smaller chance of permanent cure than others.

There is a direct relationship between the percentage of operability, of operative mortality, and of the permanent cures. The surgeon who has a high percentage of operability, that is, who operates on the more extensive cases, has a higher percentage of deaths from the operation and a lower percentage of permanent cures than the man who operates only on more favorable cases. By operating on the extensive cases, however, there is a larger absolute number of permanent cures because some cases are saved that otherwise would be lost. In some European clinics as high as 78 per cent. operability is reported; the average for all clinics, however, is probably not over 40 per cent. In America the percentage of operability is still less. In a series of about 80 cases reported to the health department of a large American city as having died of carcinoma of the uterus, only 25 per cent. had had an operation for the cure of the lesion. In the whole country the percentage would be much less.

Operation.—For the operable case of carcinoma of the cervix uteri, as it has been defined under this heading, the removal of the uterus is the operation which promises the best immediate and permanent result to the patient and is therefore indicated. The removal of the uterus is done either by the abdominal or vaginal route. By each route there are two general methods depending on the amount of cellular tissue that is removed. These operations are usually designated as "simple" and "radical" hysterectomies. That is, the operations for carcinoma of the cervix or fundus uteri are:

1. Radical abdominal hysterectomy.
2. Simple abdominal hysterectomy.
3. Radical vaginal hysterectomy.
4. Simple vaginal hysterectomy.

A radical abdominal hysterectomy is the removal of the uterus and the appendages together with as much as possible of the pelvic connective tissue and also the iliac glands. The operation is frequently designated as Wertheim's operation, though the general principles were first described by Clark and Ries. The operation is extensive, necessitating the exposure of the ureter on each side, and is associated with a high operative mortality ranging from 10 per cent. to 25 per cent. This operation should be done for carcinoma of the cervix uteri only in cases that are favorable surgical risks; it should not be done on patients with cardiac, pulmonary, renal, or other general lesions which in themselves would add to the risk of the operation. A thick abdominal wall adds to the difficulty of the operation, and may contra-indicate it on account of the increased risk.

The radical abdominal hysterectomy is the operation of first choice for carcinoma of the cervix uteri.

The radical abdominal hysterectomy should be performed for carcinoma of the fundus uteri only in exceptionally favorable cases if at all. A carcinoma of the cervix uteri extends comparatively early to the cellular tissue about the cervix uteri, and it is the removal of this cellular tissue that is accomplished by the radical operation and for which the high operative risk is assumed. A carcinoma of the fundus uteri extends toward its peritoneal coat and does not involve the pelvic cellular tissue until late. In most cases there is probably an involvement of the peritoneum and some abdominal viscera before there is an extension into the broad ligaments. The advantage gained, therefore, by the radical operation is not sufficient to warrant the greater operative mortality.

The simple abdominal hysterectomy is the removal of the uterus and the appendages, but without any

definite attempt to remove any of the pelvic connective tissue. The operation is indicated in cases of carcinoma of the cervix uteri which are unfavorable for the radical abdominal operation and for practically all operable cases of carcinoma of the fundus uteri. The operation is easier than the radical operation, and is associated with a much lower operative mortality.

As no attempt is made to remove any of the pelvic cellular tissue around the cervix the operation is practically limited to those cases in which there has been little or no involvement of the broad ligaments. In other words, many cases of carcinoma of the cervix uteri are operable only by a radical operation.

In a radical vaginal hysterectomy the vagina is enlarged by a paravaginal incision, and the uterus and appendages with a liberal amount of cellular tissue are removed. The operation is one that is rarely performed in America. Its strongest advocate is Schauta, of Vienna. The chief advantage claimed for the operation is a lower primary mortality than from the radical abdominal operation. A disadvantage claimed for it is that the iliac lymphatic glands cannot be examined and removed if found diseased.

A simple vaginal hysterectomy was formerly the usual operation for a carcinoma of either the cervix or fundus uteri. It is associated with a low primary mortality, but with a greater risk of scattering cancer cells during the manipulation of the uterus and of the implantation of cancer cells in the vaginal wound during the operation. It is the operation to be selected in a patient with a thick abdominal wall and a large vagina or with a prolapse of the uterus.

3. Inoperable Cases.—Probably 75 per cent. at least of the cases of carcinoma of the cervix uteri and of the fundus uteri are inoperable at the time that they are seen by competent surgeons; that is, they have passed the stage when the uterus can be removed with any hope of permanently curing the patient. Unfortu-

nately on account of local recurrences a large part of the cases that are subjected to operation are ultimately in this same inoperable class. While there may be no hope of permanently benefiting these cases, their lives can be prolonged and made far more comfortable by appropriate treatment. The irregular bleeding and the foul discharge can often be controlled so that they are not troublesome symptoms even during the terminal stages of the disease.

Cauterization.—This is by far the best treatment for an inoperable carcinoma of the cervix uteri. It is applicable to the early stage of inoperable cases. There is little or nothing to be gained by cauterizing the advanced stage after the vaginal walls have been largely involved or there has been an ulceration into either the vagina or the rectum.

The use of the cautery in the treatment of carcinoma of the cervix uteri was strongly advocated by Byrne, of Brooklyn, about 1892. He used it in the early as well as in the more advanced cases, and his end-results compare favorably with most operative results at the present time. More recently Percy has perfected Byrne's technique principally by the introduction of the hand of an assistant into the abdominal cavity to guide the operator in the use of the cautery. Byrne and also Percy urge that the cautery should not be at too high a degree of heat, as by a lower degree of heat and deeper penetration, cancer cells in tissue otherwise normal may be destroyed without permanent injury to the tissue itself. Percy advocates the use of the cautery for cases that most surgeons would consider suitable for a hysterectomy. He uses it not only as a palliative measure to relieve symptoms but also as a curative method. Most surgeons use the cautery alone on cases that are considered inoperable, or to sterilize the growth previous to its removal by operation.

Caustics.—Chloride of zinc is the caustic most frequently used in the treatment of carcinoma of the cervix uteri. It may be used by applying pieces of cotton or gauze

soaked in a solution of chloride of zinc to the cervix uteri after the friable portion of the growth has been removed with the curette. Repeated applications of the caustic are necessary. By controlling the bleeding and discharge the general health of the patient may be improved.

Acetone has been recommended by Gellhorn for the treatment of inoperable carcinoma of the cervix uteri. The acetone is allowed to remain in contact with the malignant growth exposed by a speculum for five or more minutes, depending on the amount of pain caused by it. The result is to harden the tissue and to control the bleeding and discharge. Neither chloride of zinc nor acetone checks the spread of the disease.

Douches.—Simple cleansing douches such as boric acid, salt solution, etc., add to the comfort of the patient by keeping the vagina and the malignant growth clean. If the discharges are not allowed to accumulate and decompose in the vagina there is less odor. In general the odor is controlled better by keeping the parts clean than by the use of disinfectants.

Pain.—Much can be accomplished for the pain of carcinoma of the cervix uteri by keeping the growth clean. The pain is often greatly relieved by a thorough curettage and cauterization of the growth. The pain in carcinoma of the fundus uteri may be due to pieces of tissue or discharge retained in the uterus, which act as foreign bodies causing uterine contractions. This pain is relieved by a curettage which will leave a uterus that is relatively clean and with free drainage.

Sedatives are usually necessary during the inoperable stage. At first aspirin and phenacetin will control the pain. Later codeine and morphin will be necessary.

End Results.—The end results of operations for carcinoma of the cervix uteri as reported by different operators show wide variations. With the more extended radical abdominal operation, there has been a definite increase in the percentage of cures even though more extensive cases are subjected to operation.

The following table taken from Döderlein and Krönig's *Operative Gynäkologie* gives the operability, the absolute and the relative cures for a number of European operators:

RADICAL ABDOMINAL HYSTERECTOMIES.

Operator.	Operability. Per cent.	Absolute cures. Per cent.	Relative cures. Per cent.
Zweifel	51.8	23.4	45.2
Döderlein	59.7	17.0	28.0
Bumm	60.9	16.0	26.3
Krönig	78.9	25.3	32.2
Wertheim	56.0	18.3	42.4

RADICAL VAGINAL HYSTERECTOMIES.

Operator.	Operability. Per cent.	Absolute cures. Per cent.	Relative cures. Per cent.
Schauta	51.3	16.4	34.5
Staude	70.7	20.0	30.0
Thom	44.2	19.3	43.7

By "operability" is meant the percentage of cases that come under observation that are operated upon. "Absolute cures" are the percentage of cases that are seen, that are well at the end of the five-year period. "Relative cures" are the percentage of cases that are operated upon, that are well at the end of the five-year period.

These figures represent the best results that are obtained in the large European clinics and are more favorable than American results. In America the cases of carcinoma of the cervix uteri do not come under observation until a more advanced stage than in Germany and Austria. The percentage of "relative" cures following the radical abdominal operation in America is under 15 per cent. The percentage of "relative cures" following the simple abdominal or vaginal hysterectomies is distinctly less than 10 per cent. This is an unfortunate showing for a disease, which, if recognized early could be cured in most cases.

The end results of operations for carcinoma of the fundus uteri are by far more favorable than those of car-

cinoma of the cervix uteri. This is true of American as well as of European clinics. The following table, adapted from Döderlein and Krönig, gives the percentages of cures following operations for carcinoma of the fundus uteri, of a number of European operators:

Olshausen	40.0 per cent.
Leopold	100.0 "
Pfannenstiel	86.8 "
Zweifel	77.7 "
Kaltenbach	66.6 "
Döderlein	100.0 "

The reasons for these more favorable results have already been given.

Causes of Death Following Operation.—Nearly one-half of the deaths following the radical abdominal operation for carcinoma of the cervix uteri are due to some form of sepsis. Of 93 deaths in Wertheim's series of 500 cases there were 39 deaths, or 42 per cent., from peritonitis. The source of the sepsis is the infected malignant growth in the cervix, which is practically impossible to completely sterilize.

There were twenty-two deaths, or 24 per cent., from feeble heart and cachexia. These deaths were probably due to the combination of causes which include bleeding, shock, anesthesia, etc., of a severe operation on a patient in poor general condition. The high percentage of deaths from these causes is indicative of the severity of a radical abdominal hysterectomy for carcinoma of the cervix uteri.

There were nine deaths, or 10 per cent., from pyelonephritis. In this operation each ureter is exposed and the bladder is widely separated from the uterus and vagina. Retention of urine requiring catheterization for a long period is a frequent result. The pyelonephritis is the result of these three factors, the minute injury to the bladder and ureters and the prolonged use of the catheter.

Among the other causes of death following the radical

abdominal hysterectomy for carcinoma of the cervix uteri as shown by Wertheim's series are ileus (3 cases), postoperative bleeding (2 cases), ligation of ureters (1 case), and pneumonia (2 cases).

Recurrences.—*Locality.*—In addition to metastases in distant organs, which are comparatively rare, recurrences following the removal of the uterus for carcinoma of the cervix uteri are found in two places: (1) in the scar at the top of the vagina, or in the cellular tissue immediately around it, and (2) in the lymphatic glands.

The largest number of recurrences are in the vaginal scar or in its immediate vicinity. There are two factors which influence the frequency of recurrence in this locality. The cellular tissue about the top of the vagina is that in which extension of a carcinoma of the cervix uteri regularly occurs and it is at this place that it is most difficult to work widely from the disease in removing the uterus. The other factor is the implantation of cancer cells in the cut edge of the vagina in the removal of the uterus. Great care should be used to avoid the implantation of cancer cells by destroying as much of the growth as possible with the cautery before beginning to remove the uterus. Some surgeons cut through the vaginal wall with the cautery for this same purpose. The prevention of recurrence in this vicinity is also favored by the removal of a wide cuff of vagina with the cervical growth.

Recurrence in the lymphatic glands, following the removal of the uterus for carcinoma, is infrequent. The lymphatic glands in either carcinoma of the cervix uteri or of the fundus uteri are involved late and when the glands have become involved, the local lesion is usually so extensive that the case is inoperable. When the glands are involved, they are usually the iliac glands. In some cases it may be possible to feel them under an anesthetic.

Types.—Clinically there are two distinct types of recurrence of carcinoma of the uterus—the diffuse and the circumscribed. The diffuse type is most frequent and the entire top of the vagina is infiltrated with the

growth which is beyond further operative relief. The circumscribed is rare. There is a distinct circumscribed nodule which may be movable. The important point about this type of recurrence is that frequently it can be removed by another operation. There are some cases that have remained well permanently after the removal of such a recurrence.

Time of Recurrence.—The following table, formed partly by statistics given by Döderlein and Krönig and partly from the report of Wertheim's cases, gives by years the percentage of recurrences of a number of operators following operations for carcinoma of the uterus:

	First year, per cent.	Second year, per cent.	Third year, per cent.	Fourth year, per cent.	Fifth year, per cent.
Winter . .	77.0	9.0	9.0	3.4	1.3
Seitz . . .	40.5	36.2	7.2	4.3	4.3
Wertheim .	53.0	30.0	8.0	5.0	4.0
Frommel .	35.6				
Zweifel . .	69.0				
Fritsch . .	77.0				

The percentages in this table give the years at which the recurrences were first noticed. The deaths would be at a later period. As shown by the table, the recurrences were most frequent the first year after operation, and after the second year comparatively infrequent. Recurrences may occur even after the fifth year. According to Döderlein and Krönig, in Olshausen's Clinic, two recurrences occurred in the sixth year, one in the eighth, and one in the tenth year.

CARCINOMA UTERI AND PREGNANCY.

Frequency.—This, fortunately, is a rare combination, as it is associated with greatly increased risk to the mother and to the child. Sarwey from combined statistics reported its occurrence in 0.05 per cent. of cases of pregnancy. A factor in the infrequency of the combination of carcinoma of the uterus and pregnancy is that the cancer age and the child-bearing age overlap but do not coincide. Car-

cinoma of the uterus is rare under thirty years of age and most frequent between thirty and fifty years. Childbearing is most frequent between twenty years and forty years of age and relatively rare later. It is during the common decade between thirty-one and forty years of age, which is a period when child-bearing and carcinoma of the uterus are both frequent, that the greatest number of cases of carcinoma of the uterus and pregnancy occur. Sarwey, in a study of 73 cases, found 11 per cent. between the ages of twenty and thirty years and 22 per cent. between the ages of forty-one and fifty years.

In regard to the occurrence of pregnancy with a carcinoma of the uterus there are two possibilities: One is that the carcinoma started after the inception of the pregnancy, the other is that the carcinoma existed before the pregnancy occurred. The consideration of these two possibilities must be largely on theoretical lines only. It is easy to understand that a carcinoma may start in the cervix uteri after a pregnancy has started. There is probably nothing in a pregnancy that prevents the development of a carcinoma, though such an idea formerly prevailed, and a carcinoma can develop during the months of pregnancy as well as during any other like period of time. On account of the increased activity of the pregnant uterus the carcinoma would grow with unusual activity and might reach an advanced stage of growth during the period of pregnancy.

It is probable that a pregnancy would not start after the beginning of a carcinoma of the uterus unless the malignant growth was in a very early stage, and it originated in the vaginal portion of the cervix, or in the cervical glands and did not involve the cervical canal. Later, when a cauliflower growth or an ulceration has developed on the cervix, an impregnation would seem to be practically impossible.

Pregnancy with a carcinoma of the fundus uteri probably never occurs at all or progresses only a short period. An impregnated ovum would not find a suitable place for

growth in the malignant tissue, and if it started in normal uterine mucosa beside the malignant growth the latter would soon displace it. There have been a few cases of pregnancy and a carcinoma of the fundus uteri reported in the literature, but it has been suggested that they were really cases of malignant deciduoma.

Abortion.—*Outcome of the Pregnancy.*—The outcome of the pregnancy depends on the location of the carcinoma. If it is located on the vaginal portion of the cervix or in the lower part of the cervical canal the carcinoma probably does not influence the pregnancy. As the carcinoma increases in extent and approaches the cavity of the uterus an abortion is more likely to occur. Sarwey reports 30 to 40 per cent. of abortions in cases of pregnancy associated with carcinoma of the fundus uteri.

Dystocia.—As the carcinoma increases in extent there is formed a greater barrier to the delivery of the child. When the cervix is entirely surrounded by the growth it will usually not dilate and a cervical tear must occur if the child is delivered naturally. This may be associated with an extensive hemorrhage. A rupture of the uterus may occur partly as the result of strong uterine contractions against the cervical obstruction which does not yield and partly as the result of the weakened condition of the uterus due to the malignant infiltration.

Sepsis.—Sepsis is a frequent complication following a full-term delivery or abortion when associated with a carcinoma of the cervix uteri. The explanation naturally is the septic condition of the growth, which it is practically impossible to disinfect, and the traumatism of the cervix and fundus of the uterus.

Symptoms.—Bleeding is the most constant symptom and corresponds in character to the bleeding of cancer of the cervix uteri when not complicated with pregnancy, but usually more profuse.

Prognosis.—There is to be considered the prognosis of (1) the fetus, (2) of the mother in regard to the pregnancy, and (3) the mother in regard to the carcinoma uteri.

1. *Fetus.*—As has been stated, 30 per cent. to 40 per cent. of the cases if there is no interference have an abortion or miscarriage. Of the cases that go to term, some cases may be delivered normally with no more than the ordinary risks to the child. Usually if the child is delivered through the vagina there is an increased risk on account of the cervical obstruction. If the child is delivered by a Cesarean section it is practically with no increased risk.

2. *Mother as Influenced by the Pregnancy.*—There is a greatly increased risk to the mother, if the delivery is through the vagina, from hemorrhage, sepsis, and rupture of the uterus. If the delivery is by Cesarean section, there is also some increase in the risk on account of sepsis. The complication of a carcinoma of the cervix uteri adds greatly to the risk of delivery.

3. *Mother as Influenced by the Carcinoma.*—It is generally considered that a carcinoma of the cervix uteri grows more rapidly as the result of the increased blood supply of the pregnancy. Formerly it was believed that a pregnancy interfered with the development of a carcinoma of the uterus, but this theory was probably erroneous. A carcinoma of the uterus prevents a pregnancy, but a pregnancy probably does not interfere with the development of a carcinoma.

In regard to the prognosis of the operation for the removal of a carcinoma of the cervix uteri when associated with pregnancy, there are two factors which influence it. In general, a hysterectomy during pregnancy is more easy than the removal of a non-pregnant uterus. The uterine ligaments are more relaxed, the uterus comes more easily into the abdominal wound, and is therefore more readily accessible. On the other side is the increased blood supply, and the greater tendency to hemorrhage associated with it. In general, however, the risk of removing a carcinoma of the cervix uteri is increased if it is complicated by a pregnancy.

Treatment.—The conditions which have to be considered in determining the treatment of carcinoma of the cervix uteri associated with pregnancy are the operability of the carcinoma and the viability of the child. For greater clearness of description the treatment will be considered under the following four headings:

1. Carcinoma operable, child not viable.
2. Carcinoma operable, child viable.
3. Carcinoma inoperable, child not viable.
4. Carcinoma inoperable, child viable.

1. *Carcinoma Operable, Child not Viable.*—Under these conditions the indications are to remove the uterus without special delay by the abdominal route. If the pregnancy has passed the sixth month the operation will be easier if the size of the uterus is diminished by removing the fetus and placenta before doing the hysterectomy. Under the sixth month the uterus can be removed together with its contents. A simple and not a radical abdominal hysterectomy should be performed. The decision in regard to a case with a child not viable but close to that condition may have to be decided by the wishes of the patient. With a disease progressing it would be unwise to delay unless the patient so elected. In general the child should be sacrificed in the interest of the mother.

2. *Carcinoma Operable, Child Viable.*—Under these conditions the indications are to do a Cesarean section and then to proceed at once to do a simple abdominal hysterectomy.

3. *Carcinoma Inoperable, Child Viable.*—In the interest of the mother the indication is to terminate the pregnancy; in the interest of the child it is to wait until it is viable.

In the early months the chances of the child living to term are so small and the detriment of the pregnancy to the mother is so great that the indications would be to terminate the pregnancy. This can usually be done most advantageously through the vagina after the growth has been disinfected as thoroughly as possible with the curette and cautery.

At a later period when the child is approaching viability the indication is to wait and to do a Cesarean section when the child is viable. This is safer both for the mother and the child than to deliver the child through the vagina. As the carcinoma is inoperable the additional disadvantage to the mother of the continuation of the pregnancy is more than balanced by obtaining a living child.

4. *Carcinoma Inoperable, Child Viable.*—The indication is to do a Cesarean section. The danger to the mother in this operation is from sepsis, and in some cases it would probably be best to do a supravaginal hysterectomy to remove the part most likely to become infected.

LITERATURE.

Byrne. Trans. American Gynecological Society, vol. xvii, p. 42.
Cullen. Cancer of the Uterus.
Döderlein and Krönig. Operative Gynäkologie.
Knack. Zeit. f. Krebsforsch, vol. xi, p. 463.
Percy. Surgery, Gynecology and Obstetrics, vol. xix, p. 452.

CHAPTER VII.

CARCINOMA OF THE ORAL OR BUCCAL CAVITY.

Under this heading are grouped the carcinomata of the following organs or localities:

Carcinoma of the tongue.
Carcinoma of the cheek.
Carcinoma of the palate.
Carcinoma of the gums.
Sarcoma of the jaws.
Carcinoma of the lips.

This is convenient because these structures, though anatomically separate, are so close together that two or more of the structures may be involved by the same growth, and it may not be possible to tell in which organ or locality the lesion started, even at an early stage of its development. For example, an epithelioma may begin in the mucous membrane in the angle between the tongue and the floor of the mouth, or that between the gums and the cheek. Even in its earliest stage it might involve two structures.

Etiology.—They also have certain etiological factors in common. Excessive smoking, syphilis, and broken teeth are exciting causes of cancer of the cheek as well as of the tongue. Leukoplakia is a factor predisposing to the development of an epithelioma in several places in the mouth. It is therefore best to consider all these localities together, and then each one, in some detail, separately.

Frequency.—In the year 1912, in the registration area of the United States, there were recorded 1838 deaths,

1465 males and 373 females, from cancer of the buccal cavity. At the same rate there would have been approximately 3000 deaths from this cause in the entire country, which is approximately 4 per cent. of the deaths from malignant disease of all parts of the body. In reality the total number of cases was considerably higher than the figures given. A considerable number of cases occurring in this region were permanently cured and never appeared in mortality records. On account of early diagnosis and relatively simple operations a larger percentage of cases are permanently cured in this locality, especially of the lip, than in other parts of the body. These cured cases should be added to the number given in the mortality records to correctly indicate the number of cases that actually occurred.

Sex.—Carcinoma of the buccal cavity is much more common in males than in females. This is shown both by hospital and mortality records. Of 207 cases reported by Meller from the Second University Clinic in Vienna between 1894 and 1904 there were 194, or 94 per cent. males and 13, or 6 per cent. females. Of approximately 1613 cases taken from the literature by Meller, 84 per cent. were in males and 16 per cent. in females. Of the 1838 deaths in the United States registration area during 1912, there were 1465, or 80 per cent. males, and 373, or 20 per cent. females. The greater frequency of the habit of smoking in men is one cause of the more common occurrence of cancer of the mouth in males.

Age.—In Meller's and in Steiner's series, that is, in hospital cases, the number of patients in the different decades was as follows:

	Meller's.	Steiner's.		
21 to 30 years . .	1	2	1	per cent.
31 to 40 " . .	14	13	8	"
41 to 50 " . .	46	34	24	"
51 to 60 " . .	74	54	38	"
61 to 70 " . .	58	20	23	"
71 to 80 " . .	13	2	4	"
80 " . .	1			
	207	125	98	"

The cases in Steiner's series were only of the cheek, gums, and tongue. It will be noticed that carcinoma of the mouth is decidedly more common between the ages of fifty-one and sixty years. The youngest case was twenty-four years of age, and there were only three cases, that is less than 1 per cent. under thirty years. Singer found the average of onset of 250 cases of carcinoma of the oral cavity to be 56.2 years.

The ages by decades of the 1838 cases reported in the registration area of the United States for the year 1912, that is of mortality not of hospital records, are given in the following table:

	Cases.	Per cent.
39 years	108	5
40 to 49 "	180	10
50 to 59 "	396	21
60 to 69 "	552	28
70 to 79 "	443	24
80 to 89 "	168	9
90 "	21	1

In these mortality records there were 4 cases under one year of age and 23 cases under ten years of age. These cases in early years probably were mostly of sarcoma of the soft parts, or of the bones, or of developmental defects. It will be noticed in the table that the greatest frequency was between sixty and sixty-nine years, which was one decade later than in the hospital records of Meller and Steiner. The explanation of a part of this greater age of cases in the mortality statistics is that the hospital cases were seen earlier. The mortality records were of the termination of the disease and would average two or three years later.

Smoking.—There seems to be no doubt that tobacco smoking is the first in importance of the etiological causes of carcinoma of the oral cavity. There are a number of irritating factors in tobacco smoking that influence the development of cancer. They are the chemical irritation of the tobacco smoke and the tobacco

juice, the physical irritation of the pipe, and the burning by the hot smoke or by the pipe-stem.

Tobacco smoking is probably the principal cause of the greater frequency of cancer of the buccal cavity in men than in women. Against this it is argued that carcinoma of the mouth is no more prevalent among the women of the East, with whom smoking is common, than among women of the West, with whom smoking is uncommon. Also, that the disease is by no means uncommon among those who have never smoked at all.

Clinical evidence, however, strongly supports the belief that carcinoma of the mouth is much more frequent in smokers than those who have not the habit.

Theoretically, smoking must be considered a cause of cancer of the buccal cavity. There are innumerable examples of foreign bodies held in the same place and producing a constant irritation which, beyond any reasonable doubt, have been the cause of a carcinoma. A pipe, particularly if the mouth-piece is rough, which is constantly held in practically the same place on tissue as delicate as the lip, must by analogy be considered a cause of cancer of the lip and mouth unless the theory that a constant irritation causes the growth of a cancer is discarded. If the stem is short and becomes hot there is another cause of irritation.

There is no doubt that excessive smoking causes dryness of the tongue and mouth which predisposes to the formation of cracks, fissures, and ulcers, which heal slowly. These unhealed lesions are as surely precancerous as any that exist, and must be so considered. That these lesions are caused by excessive smoking is clinically proved in many cases by the cure of the lesion as soon as the smoking is stopped. It must be accepted, therefore, that there is ample theoretical and clinical proof that smoking does predispose to the development of cancer of the mouth.

A further influence of tobacco smoking in the development of cancer of the mouth is its relationship to leuko-

plakia bucallis. This will be considered later under leukoplakia.

Syphilis.—The mouth is a frequent location for syphilitic lesions, and beyond doubt they predispose to the formation of cancer. Syphilis, smoking, and broken teeth are the three most frequent etiological factors of carcinoma of the oral cavity.

Singer studied 93 cases of oral carcinoma in relation to syphilis and found that there were certainly 35 cases, or 37 per cent. and possibly 50 cases, or 53 per cent., that gave a history of syphilis. To compare these figures, he studied 436 cases of cancer, all in other parts of the body, and found certainly 15 cases, or 3.5 per cent., and at most 23 cases, or 5 per cent., with a history of syphilis. That is, there was a history of syphilis in at least 35 per cent. of the cases of oral carcinomata, compared with 5 per cent. at most of other carcinomata. These figures are strong evidence that syphilis is an important element in the causation of cancer of the mouth.

Syphilitic lesions are common in different parts of the mouth, on the tongue, the palate, the gums, the lips; no part is exempt. Scars and possibly chronic ulcers are the natural results of such lesions, and it is easy to accept theoretically that these conditions predispose to the development of cancer, and the studies of Singer are strong clinical evidence of such predisposition.

The close relationship between syphilis and cancer of the mouth has, however, been questioned, and the more exact diagnosis of syphilis that is possible by modern laboratory methods will determine the correctness of present ideas.

Chronic Irritation.—This is one of the three important factors in the production of cancer of the mouth. The organs and structures here—the tongue, the cheeks, the lips, the palate—all are more or less constantly moving, and any irregular or jagged fixed surface with which they come in contact is sure to irritate.

The most frequent cause of the irritation is broken or decayed teeth acting on the tongue or cheek. The irritation from broken or badly fitting dental plates is another example of such irritation. Another is the irritation of smoking. This may be from the pipe, from burning, and from the smoke itself, and has been considered under smoking. Still another is holding foreign bodies in the mouth. An example of this has been seen in workmen holding nails in the mouth. The East Indian habit of holding the betel nut in the cheek has been the cause of cancer of the mouth. The irritation in these cases is partly physical, but probably largely chemical from the juices extracted in the chewing.

Leukoplakia Buccalis.—This disease is known by a number of different names, such as leukokeratosis, leukoma, smoker's patch, and chronic superficial glossitis; and probably there are a number of different but closely allied conditions grouped under the one name. The condition is not common; it is seen almost exclusively in the male sex, and rarely occurs before twenty years and usually after thirty-five years of age. Syphilis, alcohol, and smoking are supposed to be the etiological causes of leukoplakia. There is an hypertrophy or thickening of the epithelium, usually of the tongue or cheek, forming a patch of a gray color. The color is not unlike that caused by the application of a stick of nitrate of silver to mucous membrane, and it has the form of a warty excrescence rather than that of an ulceration. There is usually some inflammatory reaction around and beneath the patch. The superficial epithelium may be scraped off, leaving a red surface, which tends to bleed.

Leukoplakia usually occurs on the dorsum of the tongue, but may also occur on the cheeks, lips, palate, vulva, and penis. Usually in the early stages there are one or more patches, each about 0.5 cm. in diameter. It spreads by the periphery, and later may involve a considerable part of the tongue. It follows a chronic course, resisting treatment, and may remain quiescent

for years. During this time it is not painful, and gives the patient little or no discomfort.

Leukoplakia is of interest here, as it predisposes to the formation of an epithelioma. This is true, not only of the buccal cavity, but of other parts of the body. A number of cases of epithelioma of the penis and the vulva have been preceded by leukoplakia. An important percentage of the cases of epithelioma of the tongue develop from leukoplakia. This does not mean that leukoplakia is a cancer, or that it necessarily ever becomes one; in fact we do not know the percentage of cases of leukoplakia that develop into carcinoma.

It does mean that leukoplakia is a lesion that frequently precedes the development of epithelioma, and the knowledge of this fact should require that every case of leukoplakia should be carefully watched for the first sign of a malignant change in it.

Gout.—The cancer age corresponds to that of gout, but it is not usually considered that gout predisposes to cancer.

Singer in his study of the etiology of oral cancer found an exception to this rule. In 93 cases of oral cancer, excluding all doubtful cases, there were 21, making 23 per cent., in which a history of gout was apparently clear. In 436 cases of cancer from other parts of the body, including doubtful cases, there were only 15, making 4 per cent., in which there was a clear history of gout.

Alcohol.—It is not easy to determine the influence of alcohol in the production of oral cancer. It is usually considered one of the etiological factors, and statistics would seem to indicate the correctness of this view. It is, however, not easy to separate the influence of smoking from that of alcohol, as probably only a small percentage of those who drink to an excess do not also smoke. So far, however, as alcohol, either by direct irritation or by causing gastro-intestinal disurbances, causes ulcerations or other pathological conditions in the mouth, or interferes with the healing of such lesions, it is an undoubted influence in the development of oral cancer.

CARCINOMA OF THE TONGUE.

Etiology.—*Frequency.*—Hertzler states that 5 to 7 per cent. of all malignant epithelial growths occur in the tongue. This is probably true if limited to the male cancer cases. In Bashford's mortality statistics, 5.4 per cent. of the males, 0.5 per cent. of the females, and 2.5 per cent. of the total cancer deaths were from malignant growths of the tongue.

Sex.—Carcinoma of the tongue is far more frequent in males than in females. Erlich, studying the cases in the clinic and private practice of von Eiselsberg, in Vienna, for the years 1901–1906, found only one woman in a series of 64 cases, or 1.6 per cent. Steiner found in a series of 51 cases from the University Clinic of Budapest, in 1909, only 2 cases, or 4 per cent., in females. Ryall reported 12.5 per cent. of cases in women. In Bashford's mortality statistics there were about seven times as many males as females that died of cancer of the tongue. The proportion of the two sexes must vary in a small series of cases, but probably the figures of Ryall are too high and those of Steiner a more correct average. The greater frequency of its occurrence in males is probably due to the greater prevalence of smoking and drinking.

Age.—The earliest age at which carcinoma of the tongue occurred in Steiner's series was twenty-five years. He quotes one case which occurred at the age of seventeen years. Sixty per cent. of the cases were between the ages of forty-six and sixty years.

In Bashford's statistics there were one male and two females, under twenty-five years of age in a total of 2086 deaths from cancer of the tongue.

Of Erlich's series, 15 cases occurred between the ages of forty and fifty years, 17 cases between fifty and sixty years, and 29 cases between sixty and seventy years. This period of occurrence of carcinoma of the tongue is not only that of the greatest frequency of carcinoma in

general, but also the age of excessive tobacco smoking and that of greatest irritation from broken and jagged teeth.

Syphilis.—The three most important factors in the development of cancer of the tongue are syphilis, excessive smoking, and diseased or sharp teeth. In cancer of no other organ, is the relation of cause and effect so definite as between these three etiological factors and the development of cancer of the tongue. Ryall reported a history of syphilis in 88 per cent. of his cases. Porrier, as quoted by Steiner, found a history of syphilis in 27 of a series of 32 cases. In Steiner's series only 4 per cent. gave such a history. This is a very low rate, and is an incident of a small series. With the more exact diagnosis of syphilis and the discovery of many more cases than were supposed to exist the percentage may be even higher than those given above.

The cancer may develop in a scar or an old syphilitic ulceration. The interval between the formation of the scar or the ulceration and the development of the malignant growth is subject to considerable variation. Steiner reports one case which developed eighteen months after the healing of a syphilitic lesion.

Chronic Irritation.—This is an important causative factor in the production of cancer of the tongue, and many examples due to mechanical, chemical and thermic irritations are common in the literature. A frequent form of *mechanical irritation*, one of the three most common etiological factors of cancer of the tongue, is that from a broken or jagged tooth. Erlich found broken or carious teeth present in only 10 per cent. of the cases in his series, and is doubtful of the importance of traumatism as a causative factor in the development of carcinoma of the tongue. Most observers, however, believe that it is an important factor. DaCosta has seen a case of carcinoma of the tongue of a workman, apparently the result of constantly holding nails in the mouth. Numerous cases have been reported in which the exciting cause seemed to be a broken dental plate. An example of *thermal*

irritation of the tongue is the hot smoke from a short pipe. In such a case there would be the additional irritation of the tobacco and of the pipe itself. The most common *chemical* irritant is tobacco smoking. All writers place excessive smoking with syphilis and broken teeth as the three important factors in the causation of cancer of the tongue. The smoking produces a chronic inflammation of the tongue, and the formation of small fissures or ulcers. Chemical irritants in the form of caustics used in the treatment of benign ulcerations have been reported as changing a non-malignant to a malignant growth. While one can readily accept that repeated application of a caustic could change a benign ulceration of the tongue into a malignant growth, the suspicion of such a case would be that it was an unrecognized malignant condition from the start. The practical lesson is that any ulceration of the tongue that does not quickly respond to treatment should be considered as malignant unless it is proved otherwise.

Pathology.—Practically all carcinomata of the tongue are squamous-celled or epitheliomata. When other varieties occur, they result usually from the extension of a growth which was primary in the neighboring salivary glands.

Anatomically there are three types of epithelioma of the tongue, though all are closely related. The most frequent is (1) *an ulceration* practically from the start; less frequently at first, there is (2) a *deep nodule* on the tongue which later ulcerates; finally there is (3) a *diffuse infiltration*.

1. The epithelioma may develop in a preëxisting fissure, chronic ulcer, warty growth, or patch of leukoplakia. It may be malignant from the start, and no abnormality may have been noticed either by the patient or the physician until an ulcer has formed.

2. Less frequently a nodule can be felt in the tongue, which afterward breaks down, forming an ulcer. This type sometimes appears more malignant than the ulcera-

tive. The explanation of this is probably that it is not so easily recognized, and therefore comes under observation at a more advanced stage.

3. In still other cases there is a diffuse infiltration involving a considerable portion of the tongue from the start. When the growth is located on the margin of the tongue it may have the appearance of a pedunculated growth. In other cases the ulceration is more flat and may cover most of the dorsum of the tongue.

A number of cases have been reported of two epitheliomata developing at the same time, but independently in different parts of the tongue.

Site of Growth.—Carcinoma occurs most frequently on the margin of the tongue. It may occur on the tip, the dorsum, or on the under surface. If on the under surface, it spreads quickly to the floor of the mouth. It occurs more frequently on the anterior part of the tongue than on its base.

Metastases.—It was formerly believed that the lymphatic glands were involved late in the epitheliomata of the tongue, and that the enlarged glands associated with such a lesion were not malignant, but frequently were a result of absorption from the septic ulcerated surface. This belief was theoretically but not practically correct. An epithelioma usually runs a slow course, forming metastases late. An ulcerated lesion, such as an epithelioma of the tongue, would cause an inflammatory reaction and enlargement of the lymphatic glands. It is now known that metastases occur early in this location. This is explained in part by the abundant lymphatic supply of the tongue and in part by the frequent movement of the tongue which mechanically forces the cancer cells into the tissues.

The lymphatic glands first involved depend on the location of the growth. If it is on the side or margin of the tongue the submaxillary glands are first involved and later the deep cervical glands. If the tip of the tongue is the seat of the growth, the submental glands are

the first involved. If the growth is at the base of the tongue, the deep cervical glands are first involved. It must be remembered that the lymphatic supply in this region is so abundant and intimate that any of the glands mentioned may be involved with a growth in any part of the tongue; also, that the glands on the side opposite to that on which the growth is located may be involved as well as those on the same side. Erlich found in his series that when the growth was distinctly limited to the margin of the tongue on one side, usually only the glands on that side were involved. This is an important point in the operative treatment of the disease. Metastatic deposits occur in the liver more frequently than in any other distant organ. The sublingual gland may be involved by direct extension from the primary growth and the submaxillary gland by extension from the lymphatic glands. Metastases away from the neck are rare.

Symptoms.—*Pain.*—This is the only subjective symptom that is at all marked in the early stage of the disease. It is frequently severe, neuralgic in type, and often referred to the ear of the corresponding side. This is particularly the case when the growth is toward the base of the tongue, less frequently the case if near the tip of the tongue. The pain and soreness are increased by highly seasoned and acid foods, and by mechanical irritation, as from the teeth. When the growth extends to the floor of the mouth the movements of the tongue are greatly limited. This increases the pain and interferes more and more with talking, chewing, swallowing, and the control of saliva. If the growth extends to the alveolar processes the movements of the jaws are also limited.

Salivation.—In some cases, particularly if the growth is large and in the late stages, salivation is present and adds to the discomfort of the patient.

Diagnosis.—The conditions most frequently confused with carcinoma of the tongue are syphilitic gumma, primary syphilitic lesions, and tuberculosis.

Gumma occurs most frequently on the dorsum and

toward the base of the tongue. It is rarely on the under surface and toward the floor of the mouth. There is in both conditions a tendency toward ulceration. A negative Wassermann reaction is of more diagnostic value than a positive one, because in the latter case the two diseases may exist together. If the lesion is a gumma it should yield promptly to antisyphilitic treatment, or more positive means should be employed to definitely establish the diagnosis.

A tuberculous ulceration has different characteristics than an epithelioma. The edges are less hard, and it is more frequently surrounded by a diffuse inflammation. Previous to ulceration the differential diagnosis is difficult and may be clinically impossible. In such cases it would be necessary to remove a piece for examination.

If any ulceration of the tongue is not cured, or does not show definite improvement after a short period of treatment, a piece should be removed for microscopic examination. Unless necessary, however, it is a mistake to cut into a malignant growth even to remove a piece for examination, on account of increased danger of metastases.

The increased danger of metastases, however, is less than that of delay. If the lesion is not malignant no harm results from the removal of a piece for examination. If it is malignant, as may be determined by a frozen section, immediate operation can be performed.

Course.—The disease runs a rapid course, and usually terminates if untreated within eighteen months. In the inoperable stage, on account of the limitation of the movements of the tongue, and in some cases also of the jaws, it is difficult for the patient to take the proper amount of nourishment. This leads to rapid emaciation and hastens the termination of the disease. For the same reasons the saliva mixed with the discharges from the growth are taken into the lungs and a septic pneumonia may result. By extension of the growth, or injury to it by movement of the tongue, a severe hemorrhage may

result. This hemorrhage may be difficult to control on account of the growth, and may terminate fatally.

Inanition, pneumonia, and hemorrhage are the most frequent causes of death.

Treatment.—The removal of the growth gives the only chance of cure. This means the partial or complete removal of the tongue together with the submental and submaxillary and jugular chain of lymphatic glands on both sides of the neck. If the growth is not large, and can be widely removed, and still a part of the tongue saved, it is best not to remove the entire tongue. The partial removal is a less serious operation, the part of the tongue left is of functional value, and recurrences are not apt to occur in the remaining portion of the tongue but in the lymphatic glands.

The removal of the tongue may be done through the mouth with or without an incision through the cheek, or it may be done through the floor of the mouth, or it may be done by splitting the lower jaw.

The operation for the removal of the tongue is a severe one, and it is associated with a high mortality. In the series of 25 operative cases reported by Steiner, there were 9 deaths, a mortality rate of 36 per cent. This rate is probably higher than the average. Of the 9 deaths there were 4 from pneumonia and 1 each from sepsis, erysipelas, hemorrhage, myocarditis, and collapse. Of Erlich's series of 51 cases, 13 died of the operation and 5 cases were free of recurrence at the end of three years.

End Results.—These are unsatisfactory. Of the 16 cases in Steiner's series that recovered from the operation, 9 cases died within the first year, 4 cases in the second year, and the result of 3 cases was unknown. Of the 25 cases in Steiner's series, 12 cases, or nearly 50 per cent., were operated upon within the first three months of the apparent onset of the disease. These figures are given to show the unsatisfactory end results of the operation for epithelioma of the tongue. It should not be understood that no cases are permanently cured. If the case is seen

early and subjected to a radical operation, including the removal of the lymphatic glands, there is a fair chance of a permanent cure. The chance, however, is less than for epithelioma in most other locations.

CARCINOMA OF THE CHEEK.

Etiology.—*Frequency.*—Steiner reported 61 cases of cancer of the cheek as occurring in Dollinger's clinic during a period of ten years. It was a slightly more frequent disease at that clinic than cancer of the tongue during the same period. There was a higher percentage of cases at that clinic during the period than is usually recorded, as ordinarily cancer is more common in the tongue than in the cheek.

Sex.—In Steiner's series of 61 cases there were 59 men and 2 women; that is, 3.4 per cent. females. This infrequency of epithelioma of the cheek in females corresponds closely to that of epithelioma of the tongue and other parts of the buccal cavity.

Age.—The youngest case in Steiner's series was twenty-seven years and the oldest seventy-two years. Seventy-two per cent. were between the ages of thirty-six and fifty-five years; 40 per cent. between the ages of forty-six and fifty-five years.

Chronic Irritation.—In Steiner's series, excessive smoking was a frequent etiological factor. One of the two women in the series was an excessive smoker. Kümmel considers that cancer of the cheek is more frequently the result of the irritation of broken and decayed teeth than cancer of the tongue. Leukoplakia occurs on the cheek and its influence in the development of cancer has already been considered.

Pathology.—The growth is usually an epithelioma. It tends to spread to the gums of both the upper and lower jaws, and also to the superior and inferior maxillary bones. The growth, according to Kümmel, is especially apt to

start well back on the cheek opposite a molar or wisdom tooth and to extend to the anterior pillar of the fauces and from there to both the upper and lower jaws, limiting their movements. It rarely perforates the cheek. It starts as an ulcerated area and frequently opposite a broken tooth. In Steiner's cases it occurred in 46 cases in the left cheek and in 15 cases in the right cheek.

The lymphatic glands which may be involved are first the submaxillary, the upper superficial cervical and those about the parotid gland. Later, the deep cervical glands are affected. Steiner mentioned one case in which the glands of the side opposite to the growth were involved. This, however, is not the usual rule.

Symptoms.—In the early stages the subjective symptoms are not marked and the presence of the growth is the only sign of the disease. There may be pain, increased by irritation of the teeth and the movement of the cheek. Later, when the growth is more extensive, pain is more marked, and if both maxillæ are involved the movement of the jaws is more and more limited. This leads to difficulty in taking nourishment, emaciation, and pulmonary disturbances.

Diagnosis.—A gumma is rare in the cheek. A simple ulceration resulting from diseased teeth, particularly if associated with inflammatory induration, is more frequently confused with carcinoma of the cheek. Tuberculous ulcerations and actinomycosis must also be kept in mind.

Prognosis.—Kümmel considers carcinoma of the cheek less malignant than that of most other parts of the mouth, and that it remains for a longer time a local process. This may be due to the less extensive lymphatic supply of the cheek compared with that of the tongue and floor of the mouth.

Treatment.—The only treatment is the removal of the growth and the regional lymphatic glands. It may be necessary to remove a considerable part of the cheek so that a plastic operation will be necessary to close the

opening. It is also frequently necessary to remove a part of the upper or the lower jaw.

End Results.—Of the 61 cases of Steiner's series 33 were subjected to operation. Of these cases there were 3 operative deaths, all of which were due to pulmonary complications. Fourteen cases died of recurrence within the first year, 4 other cases within four years, and one in the sixth year. Three cases were free of recurrence over three years. Of these 1 case was operated upon previous to four years and 2 cases previous to six years.

CARCINOMA OF THE PALATE.

Etiology.—*Frequency.*—Primary carcinoma in this region is relatively rare. There were only 7 cases, including those which involved the tonsils in Steiner's series during a period of ten years, which was about one-seventh the number of cases of carcinoma of the tongue. In Meller's series there were 15 cases, or 7 per cent. of the cases of carcinoma of the oral cavity during the recorded period of ten years.

Sex.—All the cases in Steiner's series were in men. In Meller's series of 15 cases there were 14 men and 1 woman.

Age.—The youngest patient in Meller's series was thirty-four years of age. Of Meller's cases 33 per cent. were between the ages of fifty and sixty years, and 33 per cent. between the ages of sixty and seventy years.

Pathology.—Histologically, carcinoma of the hard or soft palate is usually of the flat-celled variety or epithelioma. Kümmel also speaks of a carcinoma originating in the glands of the palate. Sarcoma occurs in the palate, but less frequently than in the tonsil. Epithelioma of the palate may involve by extension the tonsil, the base of the tongue, the upper jaw, and the antrum of Highmore.

The lymphatic glands involved are usually the deep cervical glands along the internal jugular veins.

Carcinoma of the hard palate frequently perforates and involves the antrum of Highmore, and it may be difficult to determine in which place the growth was primary.

A number of cases have been reported in which the growth was limited to the uvula.

Prognosis.—The disease is progressive and ultimately terminates the life of the patient. Kümmel considers that carcinoma of the palate has a relatively small degree of malignancy, grows slowly, and forms metastases late. This may be due in part to the smaller lymphatic supply and, if on the hard palate, in part to the immobility of the structure.

Treatment.—The removal of a carcinoma of the palate usually requires not only the removal of the growth but also a part of the upper jaw.

End Results.—Of 10 cases that were subjected to operation in Meller's series of 15 cases the end results were ascertained in 9 cases. Of the 9 cases, 2 cases died of the operation, 2 cases in the first year, and 2 cases in the second year of recurrence; 2 cases lived over two years.

CARCINOMA OF THE GUMS.

Etiology.—*Frequency.*—Steiner in a series from Dollinger's clinic in Budapest during ten years, reported 13 cases of carcinoma of the mucous membrane covering the alveolar processes. These were not cases in which the growth started in the bones. At the time of operation, 7 of these 13 cases had extended to neighboring parts, that is, to the cheek, lips, or hard palate. It is possible that some of these cases started at other points in the mouth and extended to the gums. During that same period there were 51 cases of cancer of the tongue; that is, epithelioma of the gums occurred with about one-quarter the frequency of epithelioma of the tongue, and is relatively a rare locality for a malignant growth to develop.

Sex.—All of the 13 cases in Steiner's series were in men. The greater frequency in the male sex corresponds with the occurrence of carcinoma in other parts of the oral cavity.

Age.—All of the 13 cases were between the ages of forty-one and sixty-six years. Nine cases, or 69 per cent., were between the ages of fifty-one and sixty years.

Pathology.—The growth is practically always of the squamous-celled type. It is always seen as an ulceration and tends to spread on to the cheek, lip, or floor of the mouth. The location of the growth in Steiner's cases was on the gums of the lower jaw in 10 cases and of the upper jaw in 3 cases. If the growth is on the lower jaw, the submaxillary and submental lymphatic glands are first involved and later the deep cervical glands. If the growth is on the upper jaw the deep cervical glands are involved.

Prognosis.—This is unfavorable even with operation. This is partly because the cases are seen late when metastases have already formed in the lymphatic glands, and partly on account of the location of the growth, which makes it difficult to remove it widely.

Treatment.—This consists of the removal of the growth with part or the whole of the jaw on the same side. The lymphatic glands should always be removed.

End Results.—Of 8 cases operated upon three years previous to the time of Steiner's report, there was one operative death, 4 cases died of recurrence within the first year, nothing known of the outcome in 2 cases, and one case died of an intercurrent disease after seven years, which makes 12.5 per cent. of permanent cures on the five years basis.

CARCINOMA OF THE LIPS.

Etiology.—*Frequency.*—In Bashford's mortality statistics, malignant growths on the lips caused 1.6 per cent. of the male and 0.7 per cent. of the total cancer deaths.

Cancer of the lip constituted about one-third of the malignant growths of the entire face. Clinical statistics would give a smaller percentage of cases occurring on the lips than mortality statistics, as a larger percentage of cancers on the face than on the lips are cured.

Sex.—Hällström reports from the literature 2937 cases, including carcinoma of the upper and of the lower lip, of which 2634, or 89.6 per cent., were in males and 303, or 10.4 per cent., were in females. Of 1683 cases of carcinoma of the lower lip alone, also reported by Hällström, 1543, or 91.7 per cent., were in males and 140 cases, or 8.3 per cent., were in females, and of 95 cases of carcinoma of the upper lip, 56 cases, or 58.9 per cent., were in males and 39 cases, or 41.1 per cent., were in females. The proportion of males to females in carcinoma of the lip (including carcinoma of the upper and lower lip) is 8.6 to 1, of the lower lip alone, 11 to 1, of the upper lip alone, 1.4 to 1. These figures show that carcinoma of the lip, especially of the lower lip, is much more frequent in males than in females; but that carcinoma of the upper lip is only slightly more frequent in males than in females.

Age.—The ages by decades of 120 cases of carcinoma of the lip, reported by Hällström are given in the following table:

30 years	6	cases.
30 to 40 "	5	"
40 to 50 "	24	"
50 to 60 "	41	"
60 to 70 "	29	"
70 to 80 "	10	"
80 to 90 "	5	"
Total	120	"

The largest number of cases was between the ages of fifty and sixty years. Practically 80 per cent. of the cases were between the ages of forty and seventy years and only 10 per cent. under the age of forty years.

In a total of 2027 cases from mortality statistics, Bashford reported only 1 case, a female, under twenty-five years of age.

Chronic Irritation.—This is probably the most common cause of carcinoma of the lip. Smoking a pipe has long been considered a form of chronic irritation which causes carcinoma of the lip. It has, however, of late been doubted that it is as important a causative factor as was formerly believed. Theoretically a clay pipe with a short stem, which is both rough and hot, might well cause a chronic irritation of the lip which would be a factor in producing a malignant growth. The smoother pipe-stems in use at present would diminish the amount of irritation from this cause.

Frequently a burn, crack, fissure, or ulcer of the lip is formed, and its healing is prevented by the movements of the lips or by constant irritation. This irritation may be from the teeth, from anything held in the mouth, or from exposure to the weather. As a result of the interference with healing a lesion previously benign is changed to a malignant condition. There are examples of carcinomata being caused in other parts of the body by repeated burns of a moderate degree, and there is little doubt that this frequently occurs on the lip.

Constant exposure to weather is another form of chronic irritation frequently given as a cause of carcinoma of the lip. Carcinoma of the lip is more common in men, such as farm laborers, sailors, etc., who are constantly exposed to severe weather conditions, than in men who work indoors. On account of severe weather the lips become dry, easily cracked, and slow to heal.

Pathology.—Carcinoma of the lip is practically always composed of flat epithelium, and is of the type of epithelioma. The primary or precancerous lesion may be a fissure, a vesicle, a hard nodule, a burn, or a simple ulcer, and is most often situated at the junction of the mucous membrane and the skin. The most frequent lesion first noticed by the patient is a small ulceration. The edges of this ulceration are elevated, and it is surrounded by an area of hard induration. The growth may extend and involve the whole lip, or to the mucous membrane of the mouth.

Lymphatic Glands.—The submental lymphatic glands are the earliest and most frequent glands to be involved. The submaxillary glands are next in order and later the more distant glands of the neck. The sublingual gland may also be involved. The lymphatic glands of the opposite side as well as those of the same side as the growth may contain metastases. Enlarged glands are not necessarily metastases. They may be enlarged as a result of infection, but this can be determined only by microscopic examination of the excised glands.

Location.—Of 1778 cases reported by Hällström, 1683 cases, or 95 per cent., were in the lower lip and 95 cases, or 5 per cent., were in the upper lip.

The following table, adapted from combined statistics reported by Hällström, gives the frequency with which different parts of the lower lip are involved.

Right angle	2.0 per cent.
Left angle	2.5 "
Middle	19.5 "
Right half	26.0 "
Left half	24.0 "
Entire lip	26.0 "
	100.0 "

It will be noticed that one-half of all cases are situated on one-half of the lip, and slightly more frequently on the right than on the left half. The actual number of these cases is larger than is indicated in the table, because the cases in which the entire lip was involved were advanced cases, and it was not possible to determine the location of the beginning of the disease. Dividing the cases which occupied the entire lip equally among the middle and the right and left halves of the lip, there would be 75 per cent., or three-quarters of the cases of carcinoma of the lower lip which started at one side of the middle of the lip. The number of cases of carcinoma of the upper lip in any series is so small that no figures can be given to show the relative frequency with which different parts of the

lip are involved, but probably they are the same as for the lower lip.

Symptoms.—*Earliest.*—The symptoms of carcinoma of the lip are the objective signs of the growth itself, as there are no constitutional or general symptoms until the terminal stage.

It is not strictly correct to speak of the symptoms of a disease before the disease exists, but the *earliest symptoms* of carcinoma of the lip should be considered to be the fissure, or burn, or ulcer, or vesicle, or nodule in which the carcinoma may develop. Not only should these lesions be looked upon as the earliest symptoms of carcinoma of the lip, but they should be treated as such. If they occur, every effort should be made to cure them promptly. If they are not quickly cured, they should be removed and subjected to microscopic examination to determine their exact nature.

The later symptoms are those of a slowly advancing malignant ulceration. The surface bleeds easily. It has a thin discharge. The edges are elevated so that the growth, though ulcerated, has a definite tumor formation.

Prognosis.—Carcinoma of the lip is of slow growth. Metastases are formed late, and then, as a rule, in the local lymphatic glands. The duration of the disease not infrequently is 3.5 to four years.

Treatment.—Under this heading should first be considered the treatment of the precancerous lesions, that is, the fissure, or burn, or nodule that may be the forerunner of a real cancer of the lip. Bloodgood has shown the importance of the immediate treatment of these conditions. The removal of them is a slight operation, it can be done under local anesthesia, and practically without risk, and they are all cured. These cases, however, must not be mixed or included in series of real cases of carcinoma of the lip. A precancerous lesion is a benign lesion, and therefore has no tendency to recur. By curing such a lesion, however, a true malignant condition may be prevented.

The treatment of a carcinoma of the lip is its radical removal at the earliest possible moment, together with the lymphatic glands which drain the involved area. The removal of the primary growth, if it is at all extensive, may require the removal of all or a considerable portion of the lip. This requires a more or less extensive plastic operation to reconstruct a new lip.

In the past, and to some extent at present, there is a tendency not to remove the lymphatic glands in the early cases, especially if they cannot be palpated, on the assumption that they are not involved. In many cases, it is true, that they are not involved, but there is no positive way to determine this except by microscopic examination of the removed glands. Operative results prove the wisdom of removing the lymphatic glands in all cases. If the case is early the removal of the barrier of glands, that is, the submental and submaxillary glands of both sides, will suffice. This can be done by an incision concealed beneath the inferior maxilla, with little or no deformity. In more extensive cases the cervical lymphatic glands must also be removed. The removal of the glands, if necessary with the superficial muscles, should be accomplished in a single mass. This may be an extensive operation, and in some cases the primary growth is removed at one operation and the cervical glands a few days later. This is not the best plan, and a two-stage operation should be avoided if possible. Statistics show a greater percentage of recurrence after two-stage than after one-stage operations. This is partly due to the more advanced state of the disease, which necessitated the two-stage operation. The removal of the cervical glands before the removal of the primary lesion has been advocated because the chance of scattering cancer cells into the system by handling the primary growth in removing it will be avoided by having the lymphatics blocked.

Following an operation the case should be carefully watched for any sign of recurrence, as frequently the

recurrence is entirely local and can be removed with permanent success.

Operative Mortality.—This depends entirely on the extent of the case. In the early stage the removal of the primary growth with the neighboring lymphatic glands is associated with practically no mortality due to the operation itself. An advanced case, necessitating an extensive neck dissection, is associated with a greater risk. In a series of 113 cases during a period of ten years reported by Hällström there was one death, or 0.9 per cent., mortality.

End Results.—These depend largely on two factors: the extent of the disease at the time of the operation and the extent and nature of the operation itself. Even with an early lesion, an operation not sufficiently radical or without proper attention to lymphatic glands does not give favorable end results. The same is true of any operation, if the lesion is an extensive one at the time of surgical interference. Hertzler states that the percentage of permanent cures of carcinoma of the lip "is not much over 25 per cent." It is not possible to state whether this estimate is correct or not. It is possible or even probable, if all different operations, by all operators, and all cases are included (and of course this is the only correct way in which to get the true percentage of permanent cures), that the percentage of 25 per cent. is approximately correct. It does not, however, do justice to the work of the best institutions. In a series of 80 cases reported by Hällström, 67.75 per cent. were well and without recurrence at the end of three years. This is probably a fair percentage of permanent cures in any series which includes all types of cases, and is large enough to furnish fair averages, and in which the radical removal of the primary growth is associated with the extirpation of the lymphatic glands. In a series which included only early cases, the percentage of permanent cures would probably be as high as 90 per cent.

CARCINOMA OF THE FACE.

Etiology.—*Frequency.*—In the United States registration area in 1912 there were 1743 deaths from cancer of the skin. In the same proportion there would have been in the entire country 2750 deaths from that cause. This was about 4 per cent. of the cancer deaths for the year. The greater part, but not all, of these cases doubtless occurred on the face, because carcinoma of the skin is relatively uncommon elsewhere. These figures, however, do not correctly represent the frequency with which carcinoma occurs on the skin, as many cases of carcinoma of the face are cured, or have such a mild degree of malignancy, that it is not the direct or recorded cause of death.

Hertzler, quoting Heiman, states that 10 per cent. of all carcinomata occur on the face.

In Bashford's mortality statistics, malignant growths of the skin of the face, lip, nose, scalp, and ear constituted 2.4 per cent. of the total deaths from cancer. There were about twice as many males as females.

Age.—The following table gives by decades the ages of 181 cases of carcinoma of the face reported by Marassovich, and shows the ages at which the condition is most frequent:

24 to 30 years	3	cases.
31 to 40 "	7	"
41 to 50 "	30	"
51 to 60 "	50	"
61 to 70 "	56	"
71 to 80 "	30	"
80 "	5	"
	181	"

It will be noticed that the largest number occurred between the ages of sixty-one and seventy years.

Of the 1743 deaths from cancer of the skin reported in the United States registration area for 1912, the largest number, 28 per cent., occurred between the ages of seventy

and seventy-nine years. There were 20 cases under ten years of age.

Sex.—Of 182 cases reported by Marassovich, 102 cases, or 55 per cent., were in males and 80 cases, or 45 per cent., were in females. Of the 1743 deaths from cancer of the skin reported in the United States registration area for 1912 there were 61 per cent. males and 39 per cent. females. The greater exposure of men to the weather, injury, and irritation probably explains the greater frequency of carcinoma of the face in males than in females.

In Bashford's statistics there were 1390 males and 637 females recorded as having died of malignant growths of the skin of the face, lip, nose, scalp, and ear. If the growths on the lip were excluded there were 874, or 60 per cent. males, and 588, or 40 per cent. females.

Chronic Irritation.—The fact that the face and hands are more frequently the seat of carcinoma of the skin than other parts of the body is doubtless due in part to the greater exposure to weather conditions and to injury. It has been shown elsewhere that sailors, farm laborers, and others who are constantly exposed to extremes of weather conditions, the heat of summer, and the cold and possible freezing of winter, are especially disposed to cancer of the face and hands.

For the 182 cases reported by Marassovich, 65 per cent. were country people and 25 per cent. more were classified as laborers.

Pathology.—There are two types of carcinomata that are found on the face, (1) superficial and (2) deep.

The *superficial type* is the basal-celled carcinoma of Krompecher and the rodent ulcer or cancroid of older writers, and is the least malignant of all carcinomata. It is usually located above a line extending from the labial fold to the ear. It is usually single, but many cases recorded are of multiple growths. The original lesion, that is, the precancerous lesion, may be a warty protuberance or a slightly elevated patch covered with scales. After a long period, frequently a number of

years, such a lesion may become malignant. The growth even then is slow, and it may be difficult, even with a microscopic examination, to determine its malignant nature. Ultimately an ulceration forms which may become extensive and involve a large area of the face. Usually it remains small, the ulceration may be covered in whole or in part by modified epithelium and seem to be healed, though the growth is extending beneath this covering.

The *deep type* is the usual epithelioma. It is most common on the lower lip, but also occurs elsewhere on the face. It is more malignant than the superficial type, but less so than most other forms of carcinomata. The earliest or precancerous lesion may be a small wart, or nodule, or fissure. The ulceration is usually the first abnormality noticed by the patient, and has the usual characteristics of a malignant ulcer. It is hard and indurated, it has prominent edges, and is covered with a thin discharge.

Lymphatic glands, in the superficial type, are usually not involved at all unless the ulceration becomes very extensive. In the deep type they are involved late in the disease.

Location.—The following table gives the location in 179 cases of carcinoma of the face reported by Marassovich, and illustrates the relative frequency with which different parts of the face are involved:

Nose	50	cases
Lower lip	47	"
Upper lip	5	"
Inner angle of eyelids	20	"
Outer angle of eyelids	9	"
Forehead	14	"
Ear	4	"
Cheek	22	"
	179	"

Most frequently the growth starts at the junction of skin and mucous membrane.

Symptoms.—They are the objective signs of the tumor, as described under pathology, and there are no subjective symptoms until an advanced stage. There is no pain or itching, and the condition is unfortunately often neglected by the patient. The two lesions most frequently confused with epithelioma of the face are syphilis and lupus.

Treatment.—This is different for the superficial than for the deep type of carcinoma.

The superficial variety has such a low degree of malignancy that an extensive removal is unnecessary. Many of these cases are cured by caustics, Roentgen rays, radium, or the cautery. If these agents are used the case requires careful watching, as sometimes the ulcer is healed superficially, but continues to extend beneath the epithelial covering. This has happened in some cases supposed to have been cured by the use of radium. Freezing with liquid air or carbonic acid snow has given excellent results. These agents are of particular value in treating carcinomata of the eyelids and the side of the nose, as they destroy the growth and leave less deformity than the removal of the growth by a cutting operation.

The treatment of the deep variety of carcinoma of the face is the same as that of carcinoma elsewhere. It is the wide removal of the primary growth with the extirpation of the neighboring lymphatic glands. The treatment of epithelioma of the lip is described elsewhere.

SARCOMA OF THE JAWS.

Etiology.—*Frequency.*—The jaws, both the upper and lower, are the bones most frequently affected by sarcomata. The upper and lower jaws are affected in about the same proportion. Hertzler states that nine-tenths of the tumors of the jaws are sarcomata.

Age.—Sarcoma in general is more common in early years than carcinoma. Scudder gives the following

percentages for age periods in a total of 148 cases from combined statistics for sarcoma of the upper, the lower, and both jaws:

1 to 10 years	8.8	per cent.
11 to 20 "	14.1	"
21 to 30 "	19.5	"
31 to 40 "	18.9	"
41 to 50 "	11.5	"
51 to 60 "	16.2	"
61 to 70 "	8.8	"
71 "	2.1	"
	99.9	"

It will be noticed that 8.8 per cent. of the cases occurred between one and ten years of age, and that nearly three-quarters of the cases were under fifty years of age. Of 26 cases reported by Scudder from the Massachusetts General Hospital, practically the same percentages for corresponding ages were given. There were 2 cases, or 8.5 per cent. under ten years of age and 19 cases, or 80 per cent. under fifty years of age.

Sex.—The two sexes seem to be attacked with the same frequency by sarcoma of the jaw. Of 32 cases reported by Scudder, 19 cases were in males and 13 cases in females. In a total of 158 cases from combined statistics reported by Scudder, including his own cases, there were 74 males and 84 females.

Trauma.—There is no doubt that a single injury to a bone is occasionally followed by a sarcoma. Sarcoma probably develops more frequently in the jaws following a trauma than in any other bone. Löwenstein records a number of cases of sarcoma of the upper and of the lower jaw which started within a few months of a single injury. He reports a case of sarcoma of the jaw which developed two months after the extraction of a tooth.

Pathology.—Sarcoma of the jaw may arise from the periosteum forming a periosteal sarcoma or from the centre of the bone forming a medullary sarcoma. Histologically the sarcoma may be of the giant-celled, round-

celled, or spindle-celled variety. Melanosarcoma also occurs, though infrequently, in the jaw. Of these varieties, as a rule, the giant-celled is the least malignant, and the round-celled and melanosarcoma are the most malignant.

In the upper jaw the bone is thin and a medullary sarcoma is rare, and the periosteal type is common. The most frequent site for a beginning sarcoma of the upper jaw is in the antrum of Highmore. In the earliest stages, when the growth is still limited to the antrum, there is no deformity to indicate its presence. Later, as the sarcoma grows, the bony wall of the antrum of Highmore may yield in any direction. In part the bone is absorbed and thinned, and in part new bone is formed over the tumor. In a still later stage, the growth may perforate through the bone into the soft parts. It may ulcerate through the cheek, though usually the skin of the face remains intact even at the termination of the disease. As a sarcoma of the upper jaw grows outward, there is an increasing swelling or fulness of the cheek. If it extends toward the orbital plate, the eyeball may become displaced. If it extends toward the nasal cavity, there is a gradual occlusion of the passage of the corresponding side. If it extends downward toward the palate process, there is first a bulging and later a perforation of the hard palate. The growth may extend backward and fill the posterior nares.

After the antrum of Highmore, the alveolar process is the most frequent location of a sarcoma of the upper jaw. In some cases sarcoma of the upper jaw starts from the periosteum as a growth in the nasal cavity.

In the lower jaw both the periosteal and medullary varieties of sarcomata are found. The medullary sarcoma is nearly always of the giant-celled type, and is of a relatively low grade of malignancy. Other varieties may occur. The medulla of the bone is progressively replaced by the growth of the sarcoma. As it develops, the bone is gradually absorbed and thinned, and at this stage crepitation may be detected by palpation. With the

growth of the sarcoma and the thinning of the bone a swelling of the jaw develops. This is at first limited to the inferior maxilla, but later may involve the soft parts.

A periosteal sarcoma of the inferior maxilla, which is more frequently of a round- or spindle-celled variety, grows around the bone but does not destroy it, as is done by a medullary sarcoma. The soft parts are involved at an earlier stage. The periosteal sarcoma is usually more malignant than the medullary variety. This greater malignancy of the periosteal sarcoma of the lower jaw is probably due to the greater frequency of the round-celled type, and to the earlier involvement of the soft parts by extension.

Lymphatic Glands.—Metastases from a sarcoma of the upper jaw occur relatively late and recurrences are usually local and not in the lymphatic glands. A sarcoma in the lower jaw probably causes metastases at an earlier stage than a similar variety of the upper jaw. These statements, however, are general and not absolute.

Metastases from a giant-celled sarcoma of the upper or of the lower jaw occur only after the disease has reached an advanced stage. It is claimed by some observers, that giant-celled sarcomata of the jaws do not form metastases at all.

Symptoms of Sarcoma of the Upper Jaw.—The *earliest symptoms* of a sarcoma of the upper jaw—that is, the symptoms that exist before there is any swelling or deformity—depend on the part of the bone in which the growth starts.

If the growth starts in the antrum of Highmore the symptoms resemble those of an empyema of that cavity. There is over the antrum an indefinite pain or soreness, and there is a persistent foul discharge, possibly bloody, from the nose. Later there is swelling of the mucous membrane of the nose and soreness and pain in the teeth.

If the growth starts in the alveolar process the earliest symptom is probably pain in the teeth. Later the teeth become loose and the gums swollen and edematous.

If the growth starts in the nasal cavity the earliest symptoms are similar to those of a nasal polyp. There is an obstruction to the nasal passages on the side of the growth, and there is a foul, often bloody, discharge.

At a later stage, if the growth starts in the antrum, the symptoms are somewhat increased in severity, but the pain is not excessive, and the symptoms are those due to the deformity and presence of the growth. The first change usually noticed is the fulness and swelling of the cheek. The pressure upward by displacing the eyeball may cause double vision. There may be some bulging toward the nose or the mouth. By examination the antrum will be found filled with a solid body.

At this later stage, if the growth started in the alveolar process, in addition to the pain and soreness, some of the teeth will probably have been extracted and the growth will be seen in the resulting cavity. In some cases it may appear between two teeth as an epulis.

In the latest stage of the disease it may be impossible to determine in which part of the superior maxilla the growth started. The swelling of the cheek is much more marked. The function of the eye and nose on the involved side may be entirely destroyed. The facial deformity that may be caused by an advanced sarcoma of the superior maxilla may be as distressing as any that occurs in surgery.

Symptoms of Sarcoma of the Lower Jaw.—The earliest symptom may be an indefinite pain in the teeth, or the formation of a growth in the cavity remaining after the extraction of a diseased tooth, or the presence of the tumor.

The later symptoms are those of the tumor. The medullary sarcoma produces a fusiform swelling that obviously involves only the bone. The outlines of the growth are definitely limited. The growth is usually neither painful nor tender. If the growth is periosteal, it is not so definitely limited to the bone itself. Although at first limited in its outlines, the growth extends to the soft parts earlier than the medullary type.

In the latest stages it is not easy to determine the location of the origin of the sarcoma. The growth may be very extensive, producing marked deformity of the face. It may ulcerate through the skin, but usually does not.

Prognosis.—The prognosis of sarcoma of the upper and of the lower jaw depends more on the type than on the location of the growth. The giant-celled sarcoma is usually the least malignant. It is of slow growth, and remains a long time as a local lesion, and it is permanently cured by a simple operation. The most malignant are the melanosarcoma and the round-celled sarcoma. The periosteal sarcoma is usually more malignant than the medullary type. The prognosis of the more malignant varieties is less favorable, though a certain percentage of them are cured.

Treatment.—This depends on the histological type of sarcoma. If it is a giant-celled sarcoma a partial operation may be performed. That is, the growth can be exposed and scraped out without the removal of the entire bone. For a growth in the antrum of Highmore this would mean the turning back of a flap of the cheek and a portion of the superior maxillary bone. The growth may then be removed with a sharp spoon.

Scudder believes that "any malignant growth, whether sarcoma or carcinoma, involving and filling the antrum, is best treated by excision of the entire upper jaw." The more extensive operation would cause a greater deformity, but would probably be safer.

In the lower jaw the growth may be reached by the removal of one or more teeth or by the removal of an area of bone at the side of the inferior maxilla. The sarcoma is then removed with a sharp spoon. The cases of partial operation should be carefully watched for any sign of recurrence, and any recurrence should be at once removed. Some of these cases are operated upon many times for recurrences, and are ultimately permanently cured. There are also cases where a complete removal of the bone, either the superior or inferior maxilla,

may be necessary on account of the extent of the disease. These cases, however, are usually round- or spindle-celled and not giant-celled sarcomata.

For the round- or spindle-celled sarcoma the removal of the bone involved is usually indicated. In the superior maxilla this means the removal of the entire bone, including in some cases the orbital plate and the eye. In the inferior maxilla the half of the bone on the side involved may be removed.

Unless apparently involved the cervical lymphatic glands are not removed if the growth is of the giant-celled type. They should be removed for round-, spindle-celled, and melanosarcoma.

Operative Mortality.—This depends on the nature and extent of the growth and the general condition of the patient. It is not easy to give definite percentages of deaths from the removal of sarcoma of either the superior or inferior maxilla, because the series of cases from any one clinic is so small that a few unusual deaths greatly increase the mortality percentage. The removal of a sarcoma without the removal of the entire bone involved is associated with only a slight risk. The removal of the superior maxilla is associated with a greater mortality than the removal of the inferior maxilla. Scudder reported from the Massachusetts General Hospital 11 cases of sarcoma of the superior maxilla, with one operative death, or a mortality of 9 per cent., and 15 cases of sarcoma of the lower jaw with no deaths.

LITERATURE.

Butlin. Diseases of Tongue.
Da Costa. Keen's System of Surgery.
Davis. Jour. Amer. Med. Assoc., lxii, No. 22, 1718; Deut. Zeit. f. Chir., cxix, 142.
Erlich. Arch. f. klin. Chir., vol. lxxxviii.
Hällström. Operations des Lippenkreben.
Hertzler. Treatise on Tumors.
Kummel. Krankheiten des Mundes.
Meller. Deut. Zeit. f. Chir., vol. lxxxiv.
Ryall. British Med. Jour., April, 1913.
Scudder. Tumor of the Jaws.
Steiner. Deut. Zeit. f. Chir., vol. xcviii.

CHAPTER VIII.

CARCINOMA OF THE ESOPHAGUS.

Etiology.—*Frequency.*—As more exact methods of diagnosis are developed, there is an increased percentage of cases of carcinoma of the esophagus recorded. Early statistics gave its frequency as a fraction of 1 per cent. of all cases of carcinoma. In the Montreal General and Royal Victoria Hospitals, as reported by McCrae, in 265 cases of carcinoma, there were 24, or 9 per cent., which were in the esophagus. This is a relatively small number, and there are no large series of clinical cases, as there are of some organs, such as the stomach, from which accurate percentages can be made. The percentages of cases found at the Montreal hospitals are approximately the same as reported recently from other institutions and probably correctly represents the frequency of carcinoma of the esophagus. The esophagus probably ranks next to the breast, uterus, gastro-intestinal tract and gall-bladder as the organ most frequently the site of a malignant growth.

Sex.—There are more cases in males than in females. Of 772 cases, as reported by Kaus in Nothnagel's series, there were 584 cases in men and 188 cases in women, that is approximately 75 per cent. males and 25 per cent. females. In Bashford's mortality statistics, the ratio was three males to one female.

Age.—In a total of 2832 cases of malignant growths of the esophagus, Bashford recorded only one male and one female under twenty-five years of age. Seventy per cent. were beyond fifty-five years of age.

Cause.—Carcinoma of the esophagus seems to be more frequently found at the narrowest points in its lumen,

and the greater irritation at these points is the possible cause. The irritation of tumors or strictures, which were originally benign, is a possible explanation of the development of some malignant growths. The same is true of esophageal pouches or diverticula. None of these causes are definitely proved, but they are the etiological factors which seem most probable and logical.

Location.—Carcinoma of the esophagus occurs most frequently at the narrow anatomical points. The fact that carcinoma is most frequent at the narrowest places in the esophagus is generally considered as suggestive evidence that irritation is a causative factor in its production. Some writers have described as many as twelve normally narrow places in the esophagus, but this is a larger number than is ordinarily recognized, and more than is of practical value. The three most important anatomical points of narrowing, aud the three places at which carcinoma most frequently occurs, are opposite at the cricoid cartilage, at the bifurcation of the trachea, and at the cardiac orifice of the stomach. No part of the esophagus is exempt from carcinoma but probably carcinoma is most frequent at the lowest of the three points or at least in the lowest third of the esophagus.

Pathology.—Carcinoma is frequent as a primary lesion but occurs also as a secondary growth. The two varieties found are the squamous-celled and the adenocarcinoma. The squamous-celled is by far the most frequent type and originates in the lining epithelium. The adenocarcinoma is more rare and develops from the esophageal glands. At first the growth bulges toward the lumen of the esophagus, later it ulcerates and by cicatricial contraction forms a stricture. The obstruction in the esophagus may be due to the encroachment of the growth on its lumen, or to the stricture, or to the spasmodic stenosis produced by the presence of the growth. Above the stricture there may be a dilatation of the esophagus. The early symptoms of carcinoma of the esophagus, as of other parts of the gastro-intestinal tract, are largely the result of the

obstruction to its lumen. Later the symptoms are due to the involvement of neighboring structures, and to the absorption of toxines of the growth itself.

Metastases.—As a rule these are formed late. It has been stated that in 50 per cent. of the cases, no metastases are found even at autopsy. This high percentage of absence of metastases has been doubted. It may have been an estimate not based on exact scientific investigation, or based on only a small series of cases, and may therefore not be accurate. There are, however, two factors that favor the correctness of the percentage, and explain the infrequency with which metastases are found. The common type of esophageal cancer is the squamous- or flat-celled variety, which ordinarily remains a local disease until a late stage, and does not form early metastases. Secondly, the malnutrition and emaciation resulting from the difficulty or inability to take the proper amount of nourishment, cause the death of the patient before the disease has advanced to the stage at which metastases are usually formed.

When the metastases do occur, and they are sometimes found in the early stage of the disease, even before marked symptoms are present, they are most frequently found in the neighboring lymphatic glands in the posterior mediastinum or in the liver. The cervical and supraclavicular lymph glands, especially on the left side, may be involved later and can be palpated.

Extension of the Growth.—The esophagus is surrounded by important structures, the involvement of which leads to definite symptoms or possibly to immediate death.

Of the *air passages*, the growth may involve and perforate into the larynx, trachea, bronchi or the lungs themselves. Perforation into the lungs would mean that there had been an involvement of the pleura with the formation of adhesions. Such a condition would lead shortly to pneumonia and death. The perforation of one of these structures is a frequent termination of an esophageal carcinoma.

Of the *vascular system*, the growth may involve one of the larger arteries, or veins, or may rarely perforate the pericardium. The involvement of a larger artery or vein would cause a fatal hemorrhage. The involvement of a small artery or vein would lead more likely to its obstruction. Perforation of the pericardium would cause death in a short time.

Of the *nervous system*, most frequently there is pressure on the sympathetic and recurrent laryngeal nerves, producing paralysis of the parts supplied by them. Paralysis of the sympathetic or of the left laryngeal nerves strongly indicates the involvement of lymphatic glands. The right inferior laryngeal is more frequently involved with the primary growth.

Symptoms.—*Early.*—Janeway, in an analysis of the first symptoms of twenty-one cases of carcinoma of the esophagus, found as follows:

Dysphagia (permanent)	10 cases.
Dysphagia (temporary)	3 "
Dysphagia and pain	2 "
Pain	2 "
Tickling in throat	2 "
Increased mucus in throat	1 "
Loss of appetite	1 "
	21 "

Dysphagia.—Janeway's table illustrates the frequency of dysphagia as a first symptom. It may at first be temporary and in attacks but usually it is permanent and progressive. There is at first difficulty in swallowing hard pieces of food, later of any solid food, then of liquids and finally it is impossible to take any or more than the smallest quantity of fluid. An attempt to swallow food brings on an attack of coughing with regurgitation of food. In some cases, especially if the malignant growth is low in the esophagus, and there is a dilatation above it, the regurgitation of food may be postponed some hours. Such food is distinguished from stomach contents by

its alkalinity, and the absence of gastric juice and the products of gastric digestion. The regurgitated food may contain blood and rarely pieces of malignant tissue from the growth.

Pain.—This is usually a late but may be an early symptom. In two of Janeway's cases it was the first symptom, that is, it preceded the dysphagia. The pain may be over the growth, or it may be confined to the back of the neck. It is usually increased by any attempt to take food.

Pressure on Nerves.—If there is paralysis of *both recurrent laryngeal* nerves there is paralysis of the vocal cords, loss of voice, and dyspnea. If only one *recurrent laryngeal* nerve is paralyzed the voice is changed but not entirely lost.

If there is paralysis of the *sympathetic* nerve, there is contraction of the pupil on the affected side from paralysis of the dilator muscle, and narrowing of the lids or ptosis.

Involvement of Air Passages.—This produces a cough with expectoration which is at first mucus but later becomes purulent. When the growth perforates the air passages, an aspiration pneumonia shortly occurs.

Emaciation.—On account of the difficulty or inability to take the proper amount of food, there is loss of flesh and strength more rapidly than with a growth of the same type elsewhere. The patient may be hungry but refrain from eating on account of the difficulty of swallowing.

Diagnosis.—This is established only by the direct examination of the esophagus. This is done by the Roentgen rays, the olive bougie, and the esophagoscope. The symptoms given above, with the exception of the involvement of nerves and air passages, are largely the symptoms of a benign as well as of a malignant stricture, and further information is necessary to establish the diagnosis of carcinoma or a malignant stricture of the esophagus.

The *Roentgen rays* by outlining the lumen of the esophagus will picture diverticula and diffuse dilatations of the

esophagus and give some information regarding external pressure on the esophagus.

The use of *bougies* is not without danger, and is not universally recommended. The danger is in the perforation of the esophagus at the site of the growth which would be followed by a fatal local infection. In no case should an instrument be introduced into the esophagus without first excluding an aneurism.

Plummer uses a silk thread as a guide for the bougie. A few inches from a spool of silk thread is coiled and swallowed by the patient, and during the same evening two or three additional yards are swallowed. The following morning, the same amount at the rate of a foot an hour is swallowed before the patient is again examined. The intention of this plan is to have the thread carried down into the intestine far enough so that it can be made taut without being withdrawn. On this thread as a guide, a bougie is threaded and passed to and through the stricture. By noting the point of obstruction, the location of the growth is determined. By the use of the bougies with tips of various sizes, the calibre of the stricture is determined. The bougie passed in this way is of value also in determining its rigidity. By using fenestrated tips, pieces of tissue for examination are sometimes brought away.

The *esophagoscope* is not a new instrument, but it recently has been perfected, and brought into more frequent use. Its use is associated with considerable discomfort to the patient, often requiring an anesthetic, especially if the growth is in the lower part of the esophagus, and requires special skill of the physician. Through the esophagoscope, a direct view of the growth and a piece of tissue for examination is obtained. It is best not to use the esophagoscope directly after the use of the bougies, on account of the traumatism and possible slight bleeding caused by this examination. The bleeding even though slight may obscure the field, and it is better to wait for a more favorable opportunity. Neither

should the esophagoscope be used as a routine method of examination for all cases. If on account of subjective symptoms the case is obviously one of advanced carcinoma, there is little to gain and considerable risk in the use of the esophagoscope, and it should therefore be avoided. In the early case, the use of the esophagoscope is the real method for a positive diagnosis.

Treatment.—The removal of a carcinoma of the esophagus is, of course, the only treatment that offers any hope of a cure of the disease. The removal of a carcinoma of the cervical portion of the esophagus should be accomplished without great risk, and with a definite chance of a permanent cure. Such cases are, however, very rare.

The removal of a growth from the thoracic portion of the esophagus has not passed the experimental stage, though it has been done successfully. Meyer, Torek, and Janeway, in America, and Sauerbruch, in Europe, have done pioneer work in intrathoracic surgery and the time is probably not distant, when a carcinoma of the thoracic portion of the esophagus can be removed with a risk that is commensurate with the benefit to be gained. Such an operation has already been successfully performed. Torek, in *Surgery, Gynecology, and Obstetrics*, June, 1913, reports "The First Successful Case of Resection of the Thoracic Portion of the Esophagus for Carcinoma." This, however, does not remove the operation from the domain of experimental surgery though it justifies the work and furnishes a promise for the future. Torek brought the upper end of the divided esophagus out in the neck in front of the sternomastoid muscle. The lower end was inverted and a gastrostomy performed. Sauerbruch was not so successful in his work, and all of his cases, reported in available literature, died either directly or indirectly from the operation.

Plummer, who has had remarkable success in the treatment of benign stricture of the esophagus by dilatation, recommends it also for malignant stenosis, as a palliative measure to relieve symptoms. By its repeated use, he

has relieved dysphagia for a number of months. It should be done with care, as otherwise there is risk of perforation or rupture of the esophagus. If the dysphagia is too great a gastrostomy may be performed. It is not easy to decide in regard to a gastrostomy. If it is put off too late, either the patient dies from the operation, though it is a simple one, or from inanition due to inability to absorb nourishment that is taken. If it is done too early, the patient has an additional period of life under rather trying conditions. When the patient begins definitely to lose weight, it will probably add to his comfort. Greater comfort for the patient can sometimes be obtained by feeding through a tube. This may be passed for each feeding or a short tube may be passed through the stricture and left in place. In the latter case a string is attached to it and fastened to the teeth so that it can be withdrawn.

For pain, the usual remedies are used. At first aspirin will give relief. Later codein or morphin hypodermically will be necessary.

LITERATURE.

Janeway. Amer. Jour. Med. Sci., cxlvii, p. 583.
Kraus. Die Erkrankungen der Speiserohr (Nothnagel's System).
McCrae. Osler's Modern Medicine.
Meyer. Surgery, Gynecology and Obstetrics, xvii, 693.
Plummer. Collected Papers, Mayo Clinic, 1911.
Sauerbruch. Technik der Thorax Chirurgie.
Torek. Surgery, Gynecology and Obstetrics, xvi, 614.

CHAPTER IX.

CANCER OF THE STOMACH.

Etiology.—*Frequency.*—There are no statistics that give exactly the percentage of deaths from cancer of the stomach that occur in any locality or country. Hospital, autopsy, and mortality records are the three sources of information used to estimate the frequency of cancer of the stomach, but none of them is sufficiently accurate to give absolute information, and the records of different institutions vary greatly, but all taken together give sufficient information to form a general idea of the frequency of the disease.

Lockwood reported that during a period of five years between 1904 and 1908 there were admitted to the medical divisions of Bellevue Hospital 84,564 cases, and of these 143 were diagnosed as cancer of the stomach. That would be about one in 600 cases. Fenwick reports figures from six general hospitals in London, and all of these gave about one case of cancer of the stomach to each 200 medical admissions. These are figures of cases that were diagnosed under favorable conditions but many of them at a time when the modern methods of diagnosis of gastro-intestinal diseases were not used, and undoubtedly more cases of cancer of the stomach were overlooked than there were of other diseases not cancer of the stomach which were included as such. Probably the estimate of some writers, that 1 per cent. of medical admissions to general hospitals are for cancer of the stomach is more nearly correct.

Autopsy statistics give even a higher percentage of cases of gastric cancer. In the combined statistics of a

large number of autopsies, about 4 per cent. of the cases were of cancer of the stomach. The value of autopsy records is limited because autopsies are made on only a small proportion of all cases that die, and the cases are always somewhat selected.

Mortality statistics are open to the objection that autopsy and pathological examinations are rarely made and diagnoses are frequently incorrect.

Cancer of the stomach, however, is easy to diagnose when it has reached the last stages, and taken all together, mortality statistics probably give us the most correct information regarding the frequency of gastric cancer.

The mortality statistics of the United States for 1912, as prepared by the census bureau, include cancer of the stomach and cancer of the liver under a single heading because they are so closely associated, and cancer of the liver is most frequently secondary to cancer of the stomach. During the year 1912, in the registration area, there were reported 18,517 deaths from cancer of the stomach and liver, which was about 40 per cent. of the deaths from cancer of all organs. In the entire United States, if the proportion of deaths from cancer was the same as in the registration area, there were about 29,500 deaths in 1912 from cancer of these organs which is a death rate of 30.8 per 100,000 population. These statistics must not be taken to indicate absolutely the frequency of death from cancer of the stomach. Cancer of the liver is rarely primary, but it is secondary not only to the cancer of the stomach but of other organs, in which primary malignant growths are entirely obscured by the secondary growths of the liver.

They are, however, probably approximately correct. Mortality statistics of some foreign countries confirm them or give a higher death rate from gastric cancer.

Hoffman has studied the mortality from cancer of the stomach and liver in the United States registration area for ten years from 1901 to 1910 limited to the population

over forty years of age, during which years about 90 per cent. of the cases of cancer of the stomach and liver occur, and gives the following table:

MALES.

	Number.	Per cent. of all cancer deaths over forty years of age.	Rate per 100,000 over forty years of age.
Liver and stomach	50,157	50.5	96.6

FEMALES.

Liver and stomach	50,388	32.6	108.2

It will be noted that the actual number of deaths from gastric cancer was practically the same in both sexes. Also that this number constituted about one-half of all deaths from cancer in males over forty years of age, and about one-third of those in females. The large number of deaths of females from cancer of the breast and the generative organs, lowers the percentage of cancer deaths from other organs in that sex.

The higher death rate of females per 100,000 population over forty years of age, is due to the difference in the number of the two sexes living at these ages.

The number of deaths reported from cancer of the stomach is increasing each year. For example, the average annual number of deaths from cancer of the stomach and liver in the United States registration area from 1901 to 1905 was 8091, or 24.7 per 100,000 population, and from 1906 to 1910 was 13,395, or 28.3 per 100,000 population, and in 1912 it was 18,517, or 30.8 per 100,000 population. Beyond doubt a part of this increase is due to more correct diagnoses, but it is generally accepted that the actual number of cases of gastric cancer is on the increase.

Sex.—Reference to the above table of Hoffman, will show that during the years 1901 to 1910 inclusive, there were about the same number of deaths from cancer of the

stomach in each of the sexes. Of the 18,517 deaths from cancer of the stomach and liver reported in the United States registration area in 1912, 9215 were in males and 9302 in females. In Bashford's mortality statistics, in which cancer of the stomach is recorded by itself, there were 7149 males and 7119 females, who died of malignant growths of the stomach.

Formerly it was believed that it was far more frequent in men that in women, but at present, because of more accurate statistics, it is generally accepted to be equally common in the two sexes.

Age.—Cancer of the stomach is a disease of adult life. Approximately 90 per cent. of all cases are between the ages of forty and seventy years and only about 2 per cent. of the cases occur before the age of thirty years. The largest number is between the ages of fifty and sixty years. After seventy years there are comparatively few cases, largely probably because there are comparatively few people living after that age. Fenwick has shown that the number of deaths from carcinoma of the stomach in a given number of people, increases up to seventy-five years of age and that then there is a slight decrease.

Heredity.—It is now generally accepted that heredity plays no part in the etiology of cancer, and this belief applies to cancer of the stomach as well as to other organs. Considering the frequency of cancer in general, the chances are that most people have a near relative who has died of cancer of some organ. It is probable that heredity has no other bearing on the presence of cancer of the stomach.

Race.—Hoffman has prepared the following table from the mortality records of the District of Columbia for the ten years ending 1910, which gives by race as well as sex and age the periods of the death rates of cancer of the stomach and liver for the period: Rates per 100,000 population.

MORTALITY FROM CANCER OF THE STOMACH AND LIVER.

Ages.	Males.		Females.	
	White.	Colored.	White.	Colored.
30 to 39 years . .	9.7	15.2	8.7	11.3
40 to 49 " . .	28.3	30.5	31.3	27.4
50 to 59 " . .	89.5	84.4	87.6	91.0
60 to 69 " . .	221.0	166.4	151.6	82.0
70 + " . .	268.0	152.3	168.5	160.6
40 +	105.5	73.1	84.5	64.5

It will be noticed by the table that cancer of the stomach and liver in males up to the age of fifty and females up to the age of forty is more frequent in the colored than in the white race, but on the average after the age of forty it is distinctly more common in the white race. These figures, which agree in general with the statements of other writers, would indicate that the usual observation that cancer is somewhat less prevalent in the colored than in the white race, is true of cancer of the stomach.

Traumatism.—It is generally accepted that cancer may follow and be the direct result of traumatism and it cannot be denied that a cancer of the stomach may result from such a cause. Carcinoma, however, is the result of frequently repeated injuries and not usually of a single injury. It is difficult to see how the stomach, protected as it is in the abdominal cavity, can receive an external injury that results in the formation of a cancer, and it is doubtful if it often occurs. This agrees with the practical experience of other writers. Lockwood mentions no cases of his own but quotes one or two cases from Osler, which, as he himself points out, were doubtless cases of preëxisting cancers without apparent symptoms previous to the injury.

From the inside the stomach is doubtless subject to the frequent repeated injury that is known in other parts of the body to cause malignant growths. It is easy to appreciate that rough, undigested pieces of food, passing through the pylorus can be a source of repeated injury to the mucous membrane and produce a malignant growth.

A gastric ulcer may be irritated by food, or it may be repeatedly injured by the movements and the changes in size of the stomach, and converted into a malignant growth. This may be in the realm of speculation, but by analogy with the formation of cancer in other parts of the body, it is probably the explanation of the formation of some gastric cancers. Fenwick speaks of cases in which a cancer has developed as the result of foreign bodies embedded in the stomach wall.

Gastric Ulcer.—The relationship that a gastric ulcer bears to a gastric cancer has long been a topic of special interest. That a gastric ulcer may change from a benign to a malignant condition is strongly suggested though not proven by comparison with external ulcerations.

It is known that an ulceration of the cheek constantly irritated by a tooth, an ulcer of the lip by smoking or of the anus by the passage of hard feces, may change its character and become malignant. In fact, there is probably no external ulceration of which there are not examples in the literature, in which the benign character changed as a result of a continued irritation, to a malignant neoplasm. It should be accepted beyond question that an internal ulceration may change in the same way, and that a gastric ulcer may become a gastric cancer.

It is more difficult to determine the percentage of cases of gastric ulcer that change to gastric cancer, and also the percentage of cases of gastric cancers which develop in a preëxisting ulcer. It is an interesting observation that the percentages which are given by different writers are constantly increasing. The earlier writers estimated the number of cases of gastric carcinoma, which were preceded by gastric ulcer, to be 3 to 5 per cent.

Smithies from a study of 566 consecutive cases of gastric tumor, which came either to operation or autopsy at the Mayo Clinic, found that 41.8 per cent. gave the early symptoms of chronic gastric ulcer; 18.7 per cent. gave the symptoms of "irregular" gastric ulcer, that is, gave early gastric symptoms which could not be con-

sidered to certainly indicate ulcer; and 32.1 per cent. gave the symptoms of gastric cancer without a history of previous gastric symptoms.

Wilson, also from the Mayo Clinic, reports the result of a series of 530 cases of gastric cancer which came either to autopsy or operation, which were studied independently by the clinician and the pathologist. In 235 cases, that is, in about 45 per cent., the clinical and pathological diagnosis of gastric cancer on previous gastric ulcer were in exact agreement. In 60 per cent. the pathological diagnosis was cancer on previous ulcer. In the remaining 40 per cent. there were included a number of cases so far advanced that evidence of possible previous ulcer was obliterated.

While these percentages have not been confirmed by other observers and are not generally accepted, the fact that a gastric ulcer is an important factor in the production of a gastric cancer must be recognized, and the importance of curing the pre-cancerous lesion, that is, the gastric ulcer, in order to avoid a possible malignant growth should be more generally accepted.

The figures given above refer to the frequency with which a gastric cancer develops on a previous gastric ulcer; they do not, however, give any idea of the frequency with which a gastric ulcer changes to a gastric cancer. Statistics showing the frequency of the change do not exist, and with our present means of diagnosis, it would be practically impossible to obtain them. The medical diagnosis of gastric ulcer must always be more uncertain than the surgical diagnosis of gastric cancer confirmed by operative or postmortem findings. It must also be remembered, as Lockwood has pointed out, that the clinical experience of a surgical clinic, to which patients go only after exhausting all other resources, is different than that of a medical clinic to which many cases go and receive permanent relief. Lockwood, without having exact figures to substantiate his general impression, expresses the belief that not more than 3 or 4 per cent. of

his cases of ulcer of the stomach subsequently develop a gastric carcinoma.

Pathology.—*Types.*—The two principal types of carcinoma of the stomach are the adenocarcinoma and the scirrhus. The *adenocarcinoma* is the more frequent type, it grows more rapidly and forms metastases earlier than the scirrhus. It may project into the lumen of the stomach as a cauliflower growth, or it may break down forming an ulcer. The *scirrhus carcinoma* is made up more largely of fibrous tissue and is of more slow growth. It is frequently the type that causes pyloric stenosis. Ulceration is frequent but less so than in the adenocarcinoma. Colloid carcinoma is a form of degeneration which may be seen in either of the other two varieties. A carcinoma of the organ may be circumscribed and limited to a part of the stomach, or it may be diffuse involving most of the stomach. In the latter case the walls of the stomach are thick and rigid and the cavity reduced in size.

Extension.—The extension of carcinoma of the stomach may take place in any of the following ways:

1. By continuity of tissue.
2. By contiguity of tissue.
3. Through the lymphatic system.
4. Through the vascular system.
5. By peritoneal transplantation.

1. By *continuity* the growth extends until it involves most or all of the stomach. At the cardiac end it may extend to the esophagus. Fenwick reports the direct invasion of the esophagus in 4.5 per cent. of his series of 131 cases. Probably many cases diagnosed as carcinoma of the cardia, particularly those which come to autopsy or are seen only after the process is well advanced, are in reality primary in the esophagus with extension to the stomach.

Extension of carcinoma of the stomach to the duodenum is even less frequent than the extension to the esophagus. Fenwick reports it in 1.5 per cent. of involvement of the duodenum in 131 cases. The infrequency of this extension

to the duodenum is an interesting observation in the action of cancer and may be due to anatomical conditions, as suggested by Fenwick, or to the influence of duodenal secretions, as has been suggested by others. Usually carcinoma respects no anatomical divisions, but extends over the nearest tissues. The influence of duodenal secretions in the prevention of the growth of cancer is an interesting hypothesis. It is not proven, but the infrequency of primary cancer of the duodenum, which is an acknowledged fact, indicates that there is some at present unknown protective agency which limits the growth of a carcinoma in that organ.

A carcinoma of the stomach begins in the mucous membrane and from there extends to involve the submucous and muscular coats and finally the peritoneum.

2. Extension by *contiguity* means the extension to other organs and structures, situated near the stomach but not normally adherent to it. As the growth of the gastric cancer nears the peritoneum, either through an inflammatory action or the irritation of the growth itself, adhesions are formed between the stomach and neighboring organs, and through these adhesions the growth extends to other organs. The pancreas, which is normally in contact with the posterior wall of the stomach, is the organ most frequently involved. Fenwick reports the pancreas involved in 16.7 per cent. of his 131 cases. A part of these, however, was the result of extension through the lymph or bloodvessels and not all by contiguity. Next to the pancreas the liver is the organ most frequently involved by extension by contiguity. It was involved in 13.7 per cent. of Fenwick's cases. It is not so closely in contact over a large area as the pancreas but is more directly connected by blood and lymph vessels. The constant movement of the liver with the respiration may interfere with the formation of adhesions. Fenwick also reports the colon involved in 5.3 per cent. and the spleen in 3.7 per cent. of his series of cases.

3. The extension of a carcinoma through the *lymphatic*

vessels is the most important from the surgical standpoint. It is the earliest form of extension by which structures outside of the stomach are involved, and is usually the only one that there is any hope of counteracting by surgical interference. When the pancreas, liver, or other organs are involved by contiguity or otherwise the case is obviously inoperable. Such, however, is not the case with all lymphatic involvement. In the early stages, the spread of the carcinoma through the lymphatic vessels is checked by the lymphatic glands. Some of the carcinoma cells are doubtless destroyed in the glands, others live and involve the glands. The extent to which the lymphatic glands of the stomach are involved in gastric cancer, has a definite influence on the immediate and remote prognosis of the case and an intimate study of them is of the greatest importance. MacCarty and Blackford have examined microscopically a large number of glands removed from 200 resected specimens of gastric carcinoma at the Mayo Clinic. They have expressed their findings and conclusions as follows:

"The negative conclusions may be summarized as follows:

"1. The size of regional lymphatic glands bears no apparent relation to the size of the primary lesion in the stomach.

"2. The size of a lymphatic gland is no criterion of the presence or absence of carcinoma.

"3. Gross diagnoses of lymphatic glands are of no value except in advanced carcinoma of the glands.

"4. The duration of symptoms bears no apparent relation to the size and extent of involvement in the lymphatic glands.

"5. The average age at operation and sex bear no direct relation to the glandular involvement.

"The positive conclusions may be summarized as follows:

"1. The average loss of weight increases with the increase in extent of glandular involvement.

"2. The immediate hospital postoperative mortality is in direct proportion to the amount of glandular involvement.

"3. The subsequent mortality is in direct proportion to the amount of glandular involvement.

"4. Carcinomatous glandular involvement is very often microscopic.

"5. The surgeon who desires to treat early carcinoma must depend upon the microscope in the hands of an experienced pathologist for early carcinomatous lymphatic involvement.

"6. The diagnosis of early carcinomatous involvement requires extensive experience in the study of the so-called precarcinomatous reaction of lymphatic glands."

This study of MacCarty and Blackford is of special value because it is based on a careful microscopic examination of a large number of lymphatic glands, removed from cases of gastric carcinoma which were still operable. The findings prove scientifically for carcinoma of the stomach, the clinical impressions held by surgeons in regard to the involvement of lymphatic glands by ulcerated malignant growths. A carcinoma of the stomach is prone to break down and ulcerate as any carcinoma located externally or in the wall of a hollow viscus. It is then infected by the common pyogenic organisms and the neighboring glands may be enlarged as the result of this infection and not necessarily by the carcinoma. It is easy also to understand theoretically the cause of the increased immediate and remote mortality associated with the greater number of glands, because the greater the number of glands the more extensive must be the operation to remove them, and the more likely that some may be overlooked or inaccessible to operative removal. In general a larger number of involved glands indicates greater malignancy and therefore greater risk of recurrence.

Next to the perigastric glands, those of the mediastinum and diaphragm are most frequently diseased. The supraclavicular glands are involved and palpable, the

left more frequently than the right, in about 4 per cent. of the cases. In addition to the lymphatic glands, any organs may be involved through the lymphatic system. The liver, the pancreas, the peritoneum and intestines, the lungs and pleura, in the order named, are the organs most frequently involved with metastatic deposits.

4. Extension through the *blood system* is less frequent than through the lymphatic vessels. The veins are more frequently involved than the arteries. The malignant growth may involve a vein and ulcerate into its lumen. The cancerous cells are then carried by the blood to any part of the body. The bloodvessels of the stomach communicate directly with the portal system and therefore the liver is the organ most often affected. The cancer cells may enter the general venous system by direct involvement by one of the systemic veins, or by the secondary involvement from a growth in the liver, or indirectly through the lymphatic system. After the general vascular system has been invaded, the dissemination of the disease through the system is rapid.

5. Extension by *peritoneal transplantation* occurs only after the growth has advanced sufficiently to involve the peritoneal covering of the stomach. Free cancer cells, or pieces of malignant tissue, are separated from the growth, and these either by gravity or by the movement of peritoneal fluids are scattered over the general peritoneal cavity. A metastatic deposit on the anterior surface of the rectum produced by peritoneal transplantation is reported by Palmer to have been found in 6.5 per cent. of a series of 435 cases of carcinoma of the upper abdominal cavity, and to have been one of the means of determining the cases to be inoperable. Such a growth is usually located on the anterior surface of the rectum, above the prostate gland in the male, and above and behind the uterus in the female. It begins of course from the peritoneal surface of the rectum, and, as is shown by the proctoscope, it does not involve the rectal mucous membrane. The condition may occur secondarily to carcinoma

of any organ after the peritoneum has been involved if the patient is still up and about. Gravity favors the deposit in the lower part of the peritoneal cavity. Obviously a growth so far advanced that a metastatic deposit is found at such a distance from the primary growth and in such a manner, is beyond successful operative removal.

Location of the Growth.—The location at which the tumor starts in the stomach has a definite bearing on its early symptoms and its treatment. The pylorus and lesser curvature of the stomach are most frequently involved first and the cardia next. The following percentages from Patterson show the location of the growth in 168 consecutive postmortem cases of gastric carcinoma:

Pylorus	61.3 per cent.
Lesser curvatures	14.2 "
Cardiac orifice	5.9 "
Anterior wall	5.3 "
Whole stomach	4.7 "
Central	4.1 "
Posterior surface	4.1 "

These figures correspond closely to those of other observers who have made their statistics from postmortem examinations. At this stage, the growth is often so far advanced that it is impossible to determine surely at what point the growth commenced. Statistics from surgical operations therefore are of greater accuracy. Surgical statistics show a larger percentage of cases starting in the lesser curvature but close to the pylorus. They also show a larger number as starting in the cardia than is indicated in the above figures.

Symptoms.—*Onset.*—In regard to the onset of symptoms cases of carcinoma of the stomach may be divided into four classes.

1. Those cases which give *no symptoms* until the disease is far advanced.

2. Those cases with a *sudden onset* following an error in diet, overexertion, traumatism or some unknown

cause. In the case with this onset, the incident which starts the symptoms, should not be considered the cause of the cancer. It is more probable that the cancer already existed, but on account of its location, or period or extent of the growth, had not given subjective symptoms sufficient to be noticed by the patient. The trauma or attack of acute gastritis, was sufficient to start abrupt symptoms which otherwise would have been present soon but which would have developed more slowly. This onset of carcinoma of the stomach is quite common.

3. Those cases with a *gradual onset* and a progressive and rather rapid course but without history of previous gastric disturbances.

4. Those cases with a *long previous history* of gastric ulcer, or other chronic disease of the stomach. It is accepted as a fact, that a carcinoma of the stomach may develop in an ulcer of the stomach, and it is natural to expect that the symptoms of the cancer of the stomach would be preceded by the symptoms of the gastric ulcer.

Early Symptoms.—As in all other internal cancers, that of the stomach may develop to an advanced stage before it gives signs or symptoms, that suggest trouble to the patient, or can be easily diagnosed by the expert clinician. Before giving any evident or marked symptoms, it may have passed the operable stage, and reached one for which nothing other than a palliative operation or the medical treatment of individual symptoms can be done for the patient. The cases of carcinoma of the stomach, in which the growth is located near the cardiac orifice, are more likely to give no early symptoms than those situated elsewhere, as they do not early interfere with its motility and digestive functions. In other cases, the early symptoms of gastric cancer are mistaken for those of some other disease. Fortunately cases of this class will become less numerous as physicians understand better and use more frequently the modern methods for the diagnosis of gastric diseases, and as the laity learns the possible significance of the symptoms of dyspepsia and gastric

disturbances, the importance of an early diagnosis and appropriate treatment, and the encouraging results of operation.

The *early symptoms* are usually pain or discomfort in the epigastric region, loss of appetite, vomiting, loss of flesh and strength.

Pain.—This is usually one of the early and most constant symptoms of cancer of the stomach. It is apt to be continuous but with exacerbations, and to increase in severity as the disease progresses. In character it is less short and severe than the pain of gastric ulcer and more of a dull, boring type. In some cases, it is more of a discomfort or distress than actual pain. The pain of gastric cancer is less influenced by the intake of food than that of gastric ulcer. More cases, however, have an increase of pain after the injection of food than do not. In gastric cancer there is usually constantly present some pain or discomfort and there are frequent exacerbations. These exacerbations of pain may come on a few minutes or some hours after taking food or may not be influenced by food at all. Lockwood considers that it is a point of diagnostic value that the pain of cancer of the stomach is less influenced by a mild bland diet than that of gastric ulcer. He considers that pain that persists after a week of peptonized milk is more likely to be caused by a cancer than an ulcer of the stomach.

Absence of pain is noted in a considerable percentage of cases of cancer of the stomach. Of Lockwood's hospital cases 21 per cent. and of his private cases 15 per cent. were free from pain. Graham reports 14 per cent. either free of pain or with only slight distress. It is probable, however, that before the termination of the disease many of these cases would develop pain and the actual number free of pain during the entire course of the disease is much less.

When pain starts, it usually continues and increases in severity. It may be relieved in rare instances by the natural formation of a gastro-intestinal fistula. This

would mean that the growth had extended through the wall of the stomach and had become adherent to a coil of the intestine and that the intervening septum had sloughed allowing the stomach contents to pass into the intestine without passing through the pylorus. Such an outcome would be most unusual and would occur only late in the course of the disease. It might relieve the pain caused by the passage of food through the pylorus but there would be considerable pain from the peritoneal involvement. If there is a narrowing of the cardiac orifice of the stomach by the growth, there may be discomfort or pain with deglutition without pain at other times. With a growth at the pylorus on account of the stenosis, sharp cramp like pains due to forcing the stomach contents through the narrow opening are common. In any of the typical locations, the growth may be painless.

The *localization* of the pain of gastric carcinoma is more indefinite than that of gastric ulcer and is also more diffuse. Most frequently the pain of carcinoma is located in the epigastrium. The pain may be referred to the lower end of the sternum, to the chest, to the shoulder or to the lower abdomen. Radiation of the pain suggests peritoneal involvement.

Vomiting.—Vomiting is a frequent symptom of cancer of the stomach. Graham gives it as a symptom in 60 to 70 per cent. of the cases. Lockwood noted it in 80 per cent. of his hospital cases, and 65 per cent. of his private cases, and explains the difference by the probable difference in the stage of the disease and attention to the diet. That is, that the private cases were seen at an earlier stage of the disease than the hospital cases. Probably at a still later stage, a larger percentage even of the hospital cases would give vomiting as a symptom. In the earlier stages of the disease vomiting is less frequent and less constant. It may be started by some error in diet and then when once started, be constant during the course of the disease. It occurs most frequently at an indefinite time varying from a few minutes to some hours

after eating. It is more indefinite as to the time of its occurrence than ulcer of the stomach and does not give the same relief to pain. The pain may be increased by vomiting.

The *location of the growth* has some effect on the time and occurrence of the vomiting. If the growth is situated at the cardiac orifice of the stomach, the vomiting may be more of the nature of a regurgitation of food. There is trouble in taking food, at first solid and later even liquids pass the cardia into the stomach only with difficulty. When the growth is situated at the fundus of the stomach vomiting is apt to appear late and to be less constant as a symptom. If situated at the pylorus, vomiting is nearly sure to begin with the stenosis and, if the latter is associated with gastric dilatation, may be in considerable quantity and at long intervals. Vomiting is apt to be an early symptom and in small quantity in the case of diffuse carcinoma of the stomach.

The *character* of the vomitus varies with the stage of the disease. In the early stages it is composed of food, more or less recently taken, partially digested and mixed with mucus. Later after the growth has ulcerated and broken down the vomitus also contains the discharges from the growth. It usually contains blood in varying amount. There may be occult blood which can be detected only by careful examination of the vomitus or blood that can easily be seen, or even blood in such amount that the life of the patient is jeopardized by its loss. A fatal hemorrhage, however, occurs from carcinoma of the stomach only rarely. Rarely pieces of the growth itself are vomited and are of positive value in making the diagnosis. In an established case the vomitus is dark brown in color, it has a foul, disagreeable odor, as would be expected from an ulcerated carcinoma, and is composed of food largely undigested and mixed with blood, mucus, and the gastric juices. In some cases the vomited matter has distinctly a fecal character. This suggests that the intestinal contents have entered the stomach,

possibly through a pylorus that is rigid and open or possibly through a gastro-intestinal fistula.

The *amount* of the vomitus has a relationship to the size of the stomach. If there is a large amount, it is suggested that there has been a dilation of the stomach probably from a stenosis of the pylorus.

Appetite.—Loss of appetite is an early and a frequent symptom of cancer of the stomach. Graham noted it in 60 per cent. of his cases. Often it is the first symptom to attract the notice of the patient. It may be for all food but is often for meat only.

Cachexia.—Loss of weight and strength are often important factors in the diagnosis of cancer of the stomach. The loss of weight and of strength is partly due to the loss of appetite and to interference with the functions of the stomach and partly to the absorption of the cancer toxins. These symptoms are usually early and progressive regardless of medical treatment, though there may be a temporary improvement of both. There is usually a distinct improvement after a gastro-enterostomy, but this also would be only temporary. The loss of flesh and strength may be the only symptom of which the patient complains, and cancer of the stomach only found after a careful detailed examination. Occasionally the interference with weight and strength does not occur until late in the course of the disease. Naturally these cases are the ones in which there has been the least interference with the appetite and the functions of the stomach, and in which there has been the least toxic absorption from the cancerous growth.

Bowels.—There is no direct connection between the condition of the bowels and the growth in the stomach. In the early stages of the disease when the functions of the stomach have been only slightly disturbed, the bowels are regular. If there is marked pyloric stenosis so that only a small amount of food passes from the stomach to the intestines, constipation is usually present. The same is often the case when on account of loss of appetite

only a small amount of food is taken. In other cases, there may be diarrhea or alternating constipation and diarrhea.

The presence of blood in the movements will be discussed elsewhere.

Blood.—The condition of the blood in gastric carcinoma differs somewhat from that usually found in cases of malignant tumors due probably to interference with the function of the stomach. In the early stages, there may be no changes in the blood. Later with the ulceration and bleeding of the growth and disturbance of the gastric functions, anemia is usually present. At first on account of the vomiting or limited intake of fluids, there may be a concentration of the blood and a corresponding increase in the number of red blood cells. Lockwood reports over 5,000,000 red blood cells in 8.7 per cent. of the cases. With this increase in the number of red blood cells there may be a low percentage of hemoglobin; that is, the percentage of hemoglobin decreases earlier and more rapidly than the number of red blood cells. Later in the majority of cases both as to hemoglobin and red blood cells, the blood gives the picture of marked secondary anemia. There is a class of cases of cancer of the stomach in which the blood picture closely resembles that of pernicious anemia.

A moderate polynuclear leukocytosis is present in most cases after the first stage. It is dependent largely on the ulceration and hemorrhage from the growth and the inflammation about it and on the metastases.

The absence of digestion leukocytosis has been noted by a number of writers. This has been noted for other gastric lesions, such as ulcer and pyloric stenosis, and also in some constitutional disturbances. It will have been seen that in the blood picture, either in the red or in the white cells, that there is nothing of more than a suggestive value.

Hemorrhage in Cancer of the Stomach.—Bleeding in a cancer of the stomach is one of the most common symptoms. It is usually divided into visible and occult bleed-

ing, and the blood may be found either in the stomach contents or in the feces. The constant presence of blood in either the stomach contents or in the feces of late years has been considered a most important diagnostic aid in cancer of the stomach.

Visible bleeding occurs in about 25 per cent. of the cases of gastric cancer. It may be vomited as a coffee-ground fluid or it may enter the intestine and be passed in the feces as tarry stools. In a small percentage of cases, probably on account of the ulceration of a large vessel, bright red blood may be vomited and the loss of blood may be sufficient to cause the death of the patient.

Occult bleeding is much more frequent than visible bleeding. Repeated examinations of stomach contents and of the feces will show occult blood in nearly every case. Care must be taken, in the examination for occult blood, to exclude other sources of blood as far as possible. In the examination of gastric contents for occult blood, bleeding from the mouth or gums and injury to the esophagus with the stomach tube are sources of possible error. In the examination of feces for occult blood, hemorrhoids, benign ulcerations of the gastro-intestinal tract, as well as certain constitutional diseases such as hemophilia and typhoid fever must also be considered. While thoroughly cooked meat does not interfere with tests, it is best to exclude all meat for two days previous to the time of examination.

If no occult blood is found on repeated examinations of the gastric contents and feces, there is probably no cancer present. If occult blood is constantly demonstrated on repeated examinations, particularly if the patient has been on a bland or milk diet, it is strongly suggestive of cancer. The occult blood of gastric ulcer is usually intermittent and usually disappears by proper diet. The occult blood of cancer is usually persistent regardless of diet. The presence or absence of occult blood, therefore, is of great diagnostic importance, but repeated examinations are necessary.

Tumor.—A palpable tumor was present in 67 per cent. of the cases in a series of 1000 cases of gastric carcinoma at the Mayo Clinic. The detection of the tumor in carcinoma of the stomach depends on the size of the tumor, the location of the tumor, and the condition of the patient.

Naturally the smaller the growth, the more difficult it is to detect it. It is, however, at this stage that its discovery is of the greatest importance as the earlier the tumor is found, the greater the chances of its still being in an operable stage. There is little to be gained by finding a tumor late in the course of the disease.

Tumors located in the cardia, in the fundus, in the posterior wall and in the lesser curvature are the most difficult to detect and in these locations may not be felt even when of large size. Tumors of the pylorus are the most easy to palpate unless they are adherent behind the liver. A thin relaxed abdominal wall and a prolapsed stomach favor the palpation of gastric tumor. A rigid or thick abdominal wall, a stomach that is adherent high and the presence of ascites tend to obscure a tumor.

The *location* of a tumor of the stomach is subject to wide variation. Most frequently the tumor is located in the umbilical or epigastric regions. The following table gives the location of cases as reported by Lockwood:

Umbilical region	38 per cent.
Epigastric region	25 "
Right hypochondriac region	19 "

The location of the tumor is influenced by respiratory movements, and by changes in size and position of the stomach due to distention either by food or for diagnostic purposes.

Unless adherent to a fixed organ, the tumor usually moves with respiration. Absence of adhesions to the liver is indicated, if at the end of a forced inspiration, which pushes the liver and tumor downward, the tumor can be grasped and held while the liver recedes.

If freely movable, there are certain changes in position

due to distention of the stomach. Tumors of the pylorus move downward and to the right. Tumors of the lesser curvature are apt to become less prominent and those of the greater curvature more prominent with distention of the stomach.

The mobility of the tumor is determined by its location in the wall of the stomach, and by the adhesions between it and other organs. If the organ to which the tumor is adherent is itself movable, the tumor of course would be also. If the tumor is adherent to the abdominal wall or to the pancreas it is not movable. If it is adherent to the liver it moves only with the liver, that is, with respiration. The opposite does not necessarily follow. A tumor may move only with the liver but not be adherent to it. If it is adherent to the colon or to the small intestines, its mobility is only slightly limited.

The mobility of the tumor is an important factor in determining the prognosis. A movable tumor indicates that the case is still operable. A fixed tumor suggests that the case is not operable. Neither statement is without exceptions. A tumor may be fixed by adhesive inflammation during the operable stage. A movable tumor may be inoperable on account of metastases, enlarged glands, or the extent of the growth.

Analysis of the Stomach Contents.—Examination of the stomach contents, revealing as it does the changes in the motor and secretory powers of the stomach and their influence on gastric digestion, is an important aid in the diagnosis of gastric cancer but, with the rare exception of a piece of the tumor itself, there is nothing pathognomonic in the findings.

Motor insufficiency is present usually early in most cases of cancer of the stomach. It may be due to the pyloric stenosis, or to the weakening of the muscle wall from toxemia, or to the infiltration of the walls of the stomach by the growth. When the motor insufficiency is marked, food, particularly solids, may remain in the stomach for a number of days. In cancer of the cardia

and the lesser curvature it is less marked than when the growth is in the pylorus or other parts of the stomach.

There may or may not be dilation of the stomach with the motor insufficiency. Lockwood believes it to be less frequent and less marked than in simple stenosis of the pylorus. It is, however, frequently present.

The most frequent changes in the secretory power of the stomach in gastric cancer is the *absence of free hydrochloric acid*. This, however, is not pathognomonic nor is it a constant finding. The absence of free hydrochloric acid was found in 56 per cent. of Graham's and in 52 per cent. of Lockwood's cases; but if present, it was usually reduced in quantity. Free hydrochloric acid may be absent in gastric neurosis and atrophy and in certain constitutional diseases, and is therefore not pathognomonic. The continued absence of free hydrochloric acid is, however, strong evidence of the presence of cancer of the stomach. The absence of the free hydrochloric acid in carcinoma of the stomach is due partly to the diminution of the amount secreted and partly to the combination of that which is secreted with products of the cancer.

Lactic acid is the organic acid most frequently found in carcinoma of the stomach. It is dependent on the diminution of hydrochloric acid and the presence of undigested albuminous food. A small amount of hydrochloric acid checks lactic acid fermentation, and as hydrochloric acid is often present in gastric carcinoma, the absence of lactic acid does not prove that cancer is not present. Lockwood reports that lactic acid, either alone or with hydrochloric acid, was present in 64 per cent. of his series of cases after the test breakfast. Other writers have found it present in a large percentage of cases.

Roentgen-ray Examination.—Roentgenology is a material aid in the diagnosis of cancer of the stomach. Its value consists in enabling the roentgenologist to detect certain mechanical and functional changes that exist in the stomach as a result of the malignant growth, and by the proper interpretation of the findings not only to assist

in making the diagnosis of gastric cancer, but also in determining the location and extent of the growth, and the advisability of operative interference. A growth involving the cardia would be considered to be inoperable either for removal or for a gastro-enterostomy. An extensive or a diffuse growth might involve so great a portion of the stomach wall, that sufficient room for a gastro-enterostomy might not remain. These facts can sometimes be determined by *x*-ray examinations, and by no other non-operative methods.

Carman states that at the Mayo Clinic, 93 per cent. of the cases of gastric cancer give diagnostic signs. He gives the following radiological signs of carcinoma of the stomach, arranged in the order of their relative importance:

1. Filling defects.
2. Altered pyloric function.
   (*a*) Gaping of the pylorus.
   (*b*) Obstruction of the pylorus.
3. Advanced position of the six-hour meal.
4. Absence of the peristaltic wave from the involved area of the stomach.
5. Diminished mobility and loss of flexibility.
6. Diminution in the size of the stomach.
7. Antiperistalsis.

1. The *filling defect* is a sign of greatest importance. It depends of course on the absence of shadow of the bismuth meal in the part of the cavity of the stomach occupied by the growth. The location, the size and the irregularity of contour of this light area indicate the location, the extent and nature of the growth. The light area projecting into the stomach shadow may be a large, rounded area with regular contour and such a condition usually indicates a gastric cancer. It may be produced by change in the shape of the stomach by external pressure, as by a tumor of one of the surrounding organs, or by feces or gas in a colon not completely emptied before the examination. The latter condition is excluded if the stomach remains the same at subsequent examinations.

It is more difficult to exclude the pressure of external tumors, particularly if they are immovable. If they are movable relative to the stomach, manipulation and a subsequent *x*-ray examination may give a different picture. That of a gastric cancer would usually be unchanged. More frequently the contour of the light area is irregular with shaded places in the shadow produced by the projections of an ulcerated irregular growth into the bismuth meal. Cole compares this light area to the appearance of finger prints. If the growth is annular, it may be indicated by a permanent change in the shape of the stomach as shown by the shape of the shadow. In the middle of the stomach, such a growth may produce an hour-glass stomach. A change in the outline of the stomach may be produced by a gastric spasm and its radiograph resemble that of a stomach contracted by a gastric cancer. Repeated examinations should differentiate between the two conditions. A diffuse carcinoma of the stomach may exist without any projections into the stomach cavity, and would cause no irregularity of the shadow. Such a stomach, however, would show interference with its normal peristaltic action and possibly also change in its size and shape.

2. *The function of the pylorus* may be altered in two opposite directions. It may be narrowed and stenosed, or it may remain permanently open and patent. The stenosis of the pylorus is caused by the encroachment and the contraction of the growth and is shown by the narrow bismuth shadow in the *x*-ray plate. The open pylorus may be caused either by infiltration and destruction of the pyloric tissues or by the decreased acidity of the stomach contents. The open pylorus is of course shown by an abnormally broad bismuth shadow in the *x*-ray plate.

3. In addition to the radiographic picture of the pylorus, the condition of the pylorus is indicated by the *position of the six-hour meal.* With an obstructed pylorus at the end of six hours there will still be a residue in the stomach.

The stomach itself may or may not be dilated. Ordinarily the head of a bismuth meal at the end of six hours is about at the cecum. In carcinoma of the stomach, due to hypermotility from the diminution of acidity it is often found at or beyond the splenic flexure.

4. The *peristalsis of the stomach* may be influenced in three ways by a gastric carcinoma. The peristaltic wave may be decreased by the diminution in acidity, it may be increased by the action of the stomach in overcoming the pyloric obstruction, it may be made irregular by the presence of the growth in the stomach wall. The last of these three is the most important.

5. *Diminished mobility* might indicate extension of the growth from the stomach to surrounding organs or to the abdominal wall. The impossibility of changing the position of the tumor or stomach by manipulation would be shown on the *x*-ray plate.

6. The *diminution* in size of the stomach without marked change in shape is sometimes found in a gastric carcinoma of the diffuse infiltrating type.

Diagnosis.—As has been repeatedly indicated, the only positive diagnosis of gastric carcinoma is the microscopical examination of a piece of the growth. Excepting in rare instances, this is never possible except after operation or autopsy. The combination of the individual symptoms is usually sufficient to establish the diagnosis more accurately than most abdominal conditions are diagnosed, and the lesions for which it is most frequently mistaken are lesions for which an abdominal operation is indicated.

The first symptom of value in establishing the diagnosis is the *presence of tumor*. A tumor is present in over one-half the cases and, reversely, most tumors in the upper abdomen are gastric carcinomata. *Evidence of pyloric stenosis* is shown by undigested food in the stomach following a test meal. The *Roentgen-ray findings* are of increasing value not only for diagnosis but for prognosis and treatment. The finding at repeated examination

of *occult blood* in stomach contents or in feces even with the patient on a bland diet is strong indication of carcinoma. The absence of *hydrochloric acid* and the presence of *lactic acid* are most frequently found.

These symptoms, of importance probably in the order named, will usually establish the diagnosis of gastric carcinoma. It will be noted that they are the result of a physical examination of the patient and of the laboratory findings and not of the subjective symptoms of the patient.

Treatment.—The three possible results for which we treat any cancer are to cure the patient, to prolong life and to relieve symptoms, and these are the objective points in the treatment of a cancer of the stomach. There is no evidence that any cancer of the stomach has ever been cured except by surgical removal, and the only treatment therefore which is of permanent value to the patient is surgical. At the present time, the number of cases that are cured is small, though cancer is more frequent in the stomach than in any other organ. Anatomically the stomach in part is more favorably placed for the radical removal of a cancer than are other organs, such as the breast and uterus which come more frequently and successfully to removal for malignant growths. Partly from the anatomical structure and relations of the stomach, and partly from the pathological character of the growth, a gastric cancer remains relatively a long time as a purely local disease, limited to the stomach or to the stomach and the lymphatic glands in its immediate vicinity. This is a great advantage in the surgical treatment of gastric carcinoma as it lowers the operative mortality and increases the percentage of permanent cures.

There are, however, certain obstacles which are difficult to overcome, and which are responsible for the small number of cured cases. The most important is that of early diagnosis. Some cases do not give evident symptoms until the disease has passed the operable stage. In other cases, though symptoms are present, they are

not sufficiently positive to compel an exploratory or other operation, and the patient is treated medically beyond the operable period. Another obstacle is the location, at the cardiac orifice, of tumors which cannot be removed by our present surgical technique. Another obstacle which is being gradually overcome is the feeling in the medical profession that the immediate and end results of gastric surgery are too unsatisfactory to urge an operation.

There are certain symptoms that show definitely that a case is inoperable. They are marked *ascites* which indicates peritoneal or hepatic involvement that is beyond relief, *cachexia,* particularly if associated with a long gastric history, and evident *metastases,* which most frequently are in the supraclavicular glands, in the rectum, at the umbilicus, or in the liver.

The treatment of cancer of the stomach will be divided into the treatment of

1. Cancer involving the pylorus.
2. Cancer involving the cardiac orifice.
3. Cancer of the middle of the stomach.

Under each of these divisions will be considered the treatment of (*a*) operable cases, that is, growths which can be removed, and (*b*) advanced cases, that is, cases on which no operation other than a palliative one can be performed.

1. Cancer of the Pylorus.—(*a*) *Operable Cases.*—These are the most favorable cases of gastric cancer for operative treatment. This consists of a pylorectomy and partial gastrectomy; that is, the removal of the pylorus and a part of the wall of the stomach with the malignant growth.

In the operation of pylorectomy and partial gastrectomy for carcinoma involving the pylorus of the stomach, about one inch of the duodenum is removed. As gastric carcinoma rarely extends on to the duodenum, this is usually sufficient. Of the stomach, that part which is situated at the right of a line drawn on the lesser curvature as near the cardiac orifice as is technically possible to the

junction of the pyloric and middle thirds or to the middle of the greater curvature, is usually removed. This would include most of the lesser curvature and a third or a half of the greater curvature. The object of this wide removal is to include the lymphatic vessels and glands of the lesser curvature and those of the pyloric end of the stomach. There are but few lymphatics in the fundus of the stomach.

In the past, with inferior surgical technique and late diagnoses, the immediate mortality and frequent early recurrences were against the operation. At present, *the immediate mortality* from the operation is materially lower and there is a larger percentage of cases that are alive at the end of five years. This is well shown by the statistics from the Mayo Clinic. Between the years of 1897 and 1910, partial gastrectomy and pylorectomy was performed 266 times (244 times for gastric cancer), with a mortality of 12.4 per cent. During the year 1909, there were 46 such operations with a mortality of 8.6 per cent. Patterson gives his mortality as about 14 per cent. These mortality percentages include cases over a period of years during which the technique of gastric surgery was in a formative stage and associated with a high mortality. With greater experience in gastric surgery and earlier diagnoses, the mortality has been lowered and until now it averages about 10 per cent. and in some clinics somewhat lower. This compares favorably with the operative mortality of carcinoma of the uterus or any other abdominal organ.

In regard to *end results* Patterson reports about 15 per cent. of the cases that recovered from the operation to be well at the end of five years. Mayo in a large series of cases, but including in part a more recent period than was covered by Patterson's series, reports that of the cases who recovered from the operation, 35 per cent. were well at the end of three years and 25 per cent. at the end of five years. These percentages are decidedly higher than the average results obtained for resection of the stomach for gastric carcinoma. It is Mayo's

opinion that both the operative mortality and the end results will be further improved, not so much by better technique or more extensive operation as by earlier diagnosis.

1. Cancer of the Pylorus.—(*a*) *Advanced Cases.*—The treatment of the advanced carcinoma of the pylorus of the stomach may be by a palliative partial gastrectomy, by a gastro-enterostomy or entirely medical.

The advocates of a *palliative partial gastrectomy* claim that there is greater relief from pain, and from toxemia due to the absorption of the products of the tumor changes, than by a gastro-enterostomy and with only a slight increase in mortality. These conditions may obtain, but probably not often. The toxemia may not be a marked symptom as, for example, in a cancer of the scirrhus type, and the pain is usually relieved by a gastro-enterostomy though possibly not with the same regularity as by a partial gastrectomy. The growth in the stomach wall may be definitely limited and easily removed, but the case may be an advanced and incurable one on account of metastatic deposits in the liver or other organ or irremovable lymphatic glands. Such a case might be suitable for a palliative partial gastrectomy as it would give more relief to the stomach symptoms than a gastro-enterostomy and with little increased risk.

A *gastro-enterostomy* is indicated and performed to relieve pyloric stenosis. By making an anastomosis between the stomach and the intestine beyond the obstruction, the stomach contents pass into the intestine without passing through the pylorus. This relieves the pain caused by the contraction of the stomach forcing its contents through the narrow pylorus, and also the pain caused by the irritation of the growth itself. A gastro-enterostomy is not indicated as soon as a diagnosis of inoperable pyloric cancer has been made, but only when the symptoms of pyloric obstruction are marked and not relieved by non-operative measures. If an advanced gastric carcinoma, which would probably ultimately cause pyloric stenosis,

has been found by an exploratory celiotomy, it would be better to do the gastro-enterostomy at that time rather than risk a second operation.

The *non-surgical treatment* is medicinal, dietetic, and mechanical. If there is absence of hydrochloric acid, its administration may assist the digestion. Pepsin practically is found to be of value in some cases. If there is hyperacidity, alkalies either as bicarbonate of soda or alkaline waters should be given. Tonics may be of benefit to the general condition of the patient. Before the termination of the disease, opium in some form will be necessary to relieve the pain. It should be remembered that the duration of the disease may be prolonged, and therefore the use of opium should be reserved for the later stages. In the beginning, much can be accomplished to alleviate pain by diet and lavage. Aspirin at first alone, later combined with codein, and finally codein alone, will postpone the necessity of using morphin.

The diet should be largely soft or liquid and with no coarse meats or vegetables. Food should be administered frequently and in small amounts. The total quantity, however, should be as liberal as the case will allow, in order to preserve the weight and general condition of the patient. The value of nutrient enemata is limited. If they are given frequently or over a long period, the rectum is apt to become irritated and be an additional cause of discomfort to the patient. Certainly fluids and probably some nourishment can be administered in this way.

Lavage is of special value in the treatment of the gastric cancer which causes pyloric stenosis to remove the stomach contents that have not passed into the intestines. Beyond keeping the stomach clean, little or nothing can be accomplished by attempting to treat the ulcerated cancer itself.

2. Cancer Involving the Cardiac Orifice.—The treatment of cancer of the cardiac orifice of the stomach is entirely palliative as the removal of the growth in this location is beyond our present surgical technique. The

symptom requiring most attention is the progressively increasing dysphagia. At first this can be relieved by soft and later by liquid foods. The danger and short duration of any benefit derived from it, excludes any attempt to dilate the stricture or to feed through the stomach tube. If the dysphagia is too marked a gastrostomy or a jejunostomy would be indicated. Lavage is excluded by the danger of passing the tube and because with the absence of pyloric stenosis there is ordinarily no indication for it.

The general medicinal and dietary treatment of these cases is practically the same as for the cases with pyloric obstruction.

3. Carcinoma of the Middle of the Stomach.—The treatment of an operable carcinoma of the middle of the stomach is practically the same as that for carcinoma of the pyloric orifice. In some cases the growth can be removed and the stomach resutured. The better operation is the partial gastrectomy and a gastro-enterostomy.

In the advanced case on account of the obstruction of the growth, a gastro-enterostomy or if there is not sufficient room, a jejunostomy may be indicated.

The general medical and dietary treatment is the same as has been described under carcinoma of the pyloric orifice.

LITERATURE.

Carman. Collected Papers, Mayo Clinic, 1913.
Cole. New York Medical Journal, February, 1914.
Fenwick. Lancet, 1901, i, 463.
Graham. Collected Papers, Mayo Clinic, 1913.
Lockwood. Diseases of the Stomach.
Martin. Osler's Modern Medicine.
MacCarty and Blackford. Annals of Surgery, June, 1912.
Palmer. Surgery, Gynecology and Obstetrics, x, 154.
Patterson. Surgery of the Stomach.
Smithies. Collected Papers, Mayo Clinic, 1913.
Wilson. Collected Papers, Mayo Clinic, 1913.

CHAPTER X.

CARCINOMA OF THE INTESTINES—SARCOMA OF THE INTESTINES—CARCINOMA OF THE APPENDIX—CANCER OF THE RECTUM.

CARCINOMA OF THE INTESTINES.

Etiology.—*Frequency.*—During the year 1912 there were in the registration area of the United States, 5923 deaths recorded from cancer of the peritoneum, intestines and rectum, that is, 12.7 per cent. of all deaths from cancer in the registration area. As cancer of the stomach and liver, the female generative organs, and of the other abdominal organs which are frequently involved in cancerous lesions, are included under separate headings, probably most of the cases of carcinoma of the peritoneum in this group were primary in the intestines, and therefore the number fairly represents the number of deaths in the United States registration area for a single year of cancer of the intestines and rectum. As the registration area for the year 1912 included 63.2 per cent. of the total population of the country, if there were proportionately the same number of deaths among the rest of the population, the total number of deaths from cancer of the intestines in the entire country for the year 1912 was approximately 9372. As during the same period in the United States registration area there were 13,517 deaths from cancer of the stomach and liver, cancer of the intestines and rectum constitute about one-third of the cases of cancer of the entire gastro-intestinal tract. In Bashford's mortality statistics, in a total of 84,448 cancer deaths there were 5723 cases, or about 7 per cent., of the malignant growths of the intestine exclusive of the rectum.

In a series of 1453 cases of cancer of the gastro-intestinal tract reported by W. J. Mayo, there were 996 cases of carcinoma of the stomach, 16 of the small intestine, 216 of the large intestine, and 225 of the rectum. That is, carcinoma of the small intestine is very rare, consisting of only 1.1 per cent. of all cases in the gastro-intestinal tract, or 3.5 per cent. of the intestinal tract; and carcinoma of the large intestine is more common, being found with approximately the same frequency as carcinoma of the rectum, and consisting of 15 per cent. of all gastro-intestinal cases. Hinz reported the combined statistics of 584 cases of carcinoma of the intestinal tract, of which 18, or 3.06 per cent., were situated in the small intestine. Brill reported combined statistics of 2128 cases of intestinal carcinoma, of which 50, or 2.3 per cent., were in the small intestine.

Sex.—Of the 5923 deaths recorded in the United States registration area from cancer of the peritoneum, intestines, and rectum during the year 1912, 2459, or 42 per cent., were in males, and 3464, or 58 per cent., were in females. These figures differ from those of most surgical clinics, as the latter record carcinoma of the intestines more frequent in males than in females. Hinz reports 48 cases of primary carcinoma of the small intestine, of which 31, or 65 per cent., were in males and 17, or 35 per cent., in females. Anschütz reports 128 cases of carcinoma of the large intestine, of which 91, or 70 per cent., were in males and 37, or 30 per cent., were in females.

In Bashford's mortality statistics, malignant growths of the intestines exclusive of the rectum were more frequently the cause of death of females than of males. Cancer of the rectum was more common in males than in females.

Considering all these statistics, it is probable that malignant growths of the intestinal tract occur with about the same frequency in the two sexes.

Age.—Carcinoma of the intestines increases rapidly in frequency after the age of forty years. Of the cases

recorded in the United States registration area in 1912, 90 per cent. were over forty years of age.

Pathology.—The most frequent form of carcinoma of the intestines is the *adenocarcinoma*. It is composed of cylindrical cells maintaining often the type of the glands. The *scirrhus carcinoma* with a preponderance of fibrous tissue is the second most common variety. The *colloid carcinoma* occurs more frequently in the intestines than in the stomach. The growths are usually single but they may be multiple.

The carcinoma may take the form of a cauliflower mass with a broad base, growing into the lumen of the intestine. Sometimes there is a growth with a small base or pedicle, suggesting that there has been a carcinomatous change in a preëxisting papilloma. This type is sometimes seen at the biliary papilla in the second portion of the duodenum. Most frequently the growth is seen as an ulcerated area with elevated edges and a necrotic, broken-down centre. This ulcerated area by extension of the growth may suddenly perforate the bowel, causing a general peritonitis. More frequently the perforation takes place slowly, and a circumscribed abscess or a communication with another viscus is formed.

The greatest tendency of the growth is to surround the intestine and to form a stricture, and the symptoms of carcinoma of the intestines are due largely to the mechanical obstruction produced by the stricture or in other ways. The growth, in addition to forming a stricture which obstructs the bowel, may grow into the lumen of the bowel and obstruct it by its size, or it may cause an intussusception, or an obstruction may be caused by a kinking of the bowel by its weight or by adhesions.

Sarcoma and lymphosarcoma of the intestines occur less frequently than carcinoma, there being in a series of autopsies only 1 case of sarcoma to 40 or 50 of carcinoma. They differ from carcinomata in occurring with about the same frequency in the small and in the large intestine, and not tending to stricture the intestines but more to a

diffuse growth. This growth may be sufficient to obstruct the bowel, but not with the same regularity as the carcinomata. The absence of obstruction makes the symptoms of sarcoma of the intestines different than those of carcinoma.

CARCINOMA OF THE DUODENUM.

In the series of 1453 cases of carcinoma of the gastrointestinal tract reported by W. J. Mayo, 16 were in the small intestine, and of these only five were in the duodenum and none of them operable. Rolleston states that in 18,000 autopsies at Guy's Hospital there were only 10 cases of primary malignant disease of the duodenum, and of these four were carcinomata.

The tendency of carcinoma of the duodenum, as of other parts of the intestine, is to form an annular stricture about the duodenum. The stricture may be sufficient to cause definite stenosis of the bowel without altering its external appearance. Occasionally the growth takes a polypoid form, especially if it starts from the mucous membrane in the vicinity of the entrance into the duodenum of the bile duct, that is, at the biliary papilla. Carcinoma starting at this point is sometimes erroneously confused with a carcinoma originating in the gall passages or in the ampulla of Vater.

Symptoms.—The symptoms of a carcinoma of the duodenum are caused largely by two mechanical obstructions, one to the intestine, interfering with the passage of the intestinal contents, the other to the common opening of the bile and pancreatic ducts, interfering with the passage of the bile and pancreatic juice into the intestines. They differ, therefore, whether the growth is located in the first, second, or third part of the duodenum, or, more accurately, whether it is located above, around, or below the ampulla of Vater. If the growth is above the ampulla of Vater, the bile and pancreatic juice pass as usual into the intestine. If the growth involves the

ampulla of Vater there may be complete or intermittent obstruction or infection of the bile and pancreatic ducts. If the growth is below the ampulla of Vater the bile and pancreatic fluids pass imperfectly through the intestinal stricture, and are to be found in the stomach contents.

Carcinoma of the *first part of the duodenum* alone occurred, as reported by Rolleston in a series of 40 cases, in 8 cases, and together with the second part in 5 more. The symptoms closely resemble those of carcinoma of the pylorus of the stomach so far as the obstruction is concerned. The stomach may be dilated and contain food remnants. Hydrochloric acid is usually not absent. A tumor may be palpated in some cases. The correct diagnosis between carcinoma of the first part of the duodenum and the pyloric orifice of the stomach is rarely made except at operation or autopsy. The absence of bile and pancreatic juice in the contents of the stomach is a characteristic sign which may help to distinguish it from carcinoma lower in the duodenum.

Carcinoma of the *second part of the duodenum*, if situated above the ampulla of Vater, gives the same symptoms as if situated in the first part; if situated below the ampulla of Vater, it gives the symptoms as if situated in the third part; if situated about the ampulla of Vater, it gives symptoms of intestinal obstruction and symptoms of obstruction and possibly inflammation of the biliary passages. In the series of 40 cases of carcinoma of the duodenum reported by Rolleston, 24 were limited entirely to the second portion and 5 others involved both the first and second parts; that is, the second part of the duodenum, particularly around the biliary papilla, is the most common location of a carcinoma of the duodenum.

The involvement of the biliary papilla by a carcinoma of the duodenum causes jaundice, enlargement of the gall-bladder, clay-colored movements and high-colored urine by the obstruction of the outflow of bile into the intestine. By ulceration of the growth, this obstruction may be relieved and the symptoms temporarily subside. In car-

cinoma of the gall passages, if the ampulla of Vater and of the head of the pancreas are involved, these symptoms are progressive and continuous and not intermittent, as they frequently are in carcinoma of the second portion of the duodenum.

With the extension of the growth, there is a catarrhal duodenitis and an inflammatory involvement of the bile passages, giving tenderness and enlargement of the liver and increase in the temperature and pulse, that is, the signs of acute infection. A suppurative inflammation of these ducts may be the cause of death.

Carcinoma of the *third part of the duodenum* occurred in only 3 of the 40 cases reported by Rolleston and is therefore the least frequent location of cancer of the duodenum. The symptoms are those of intestinal obstruction which progresses as the stenosis increases. In the early stages of the disease, bile and pancreatic fluid would be mixed with the intestinal contents which pass the stricture, so the color of the movements may not be changed. Later the movements will be light or clay-colored. As the growth is below the ampulla of Vater, both bile and pancreatic fluid may be found in the stomach contents.

Prognosis.—The prognosis of carcinoma of the duodenum is unfavorable largely on account of the difficulty of the diagnosis. Of the 5 cases of carcinoma of the duodenum and 2 of the duodenojejunal angle reported by Mayo, all were inoperable.

Treatment.—The only treatment of carcinoma of the duodenum which offers any possibility of permanent relief to the patient is the surgical excision of the growth, and this is possible only in the early stages of the disease. The location and the anatomical relations of the duodenum make the removal of a growth more difficult than from any other part of the intestine. If removal is not possible, a gastrojejunostomy may be indicated to relieve the symptoms of obstruction.

CARCINOMA OF THE JEJUNUM AND ILEUM.

Carcinoma of the jejunum and ileum are very rare, though they constitute a large part of the total length of the intestinal tract. There are various causes suggested for the rarity of carcinoma of the small intestine compared with the large intestine. Probably the fluid condition of the intestinal contents and the absence of angles for resistance to its progress are the most important factors. By analogy intestinal ulcers, as from typhoid fever or dysentery or their scars, would influence the development of a carcinoma but the recorded cases are too few to prove the assumption.

Symptoms.—If there is no stricture, there are no local signs and the symptoms are those of carcinoma in general. If there is a stricture, in addition to the general symptoms of carcinoma, there are the local symptoms due to the intestinal obstruction. As the intestinal contents are fluid, the signs of obstruction do not develop as early in the course of the disease as in the large intestine. The bowels may be constipated or alternating with diarrhea. A tumor may be present but it is not easy to distinguish it from one in the large intestine. There may be blood in the movements. The Roentgen-ray picture may be of considerable assistance in locating the stricture particularly if repeated examinations are made.

Prognosis.—As local symptoms usually develop late, few cases are seen early enough to be relieved by a radical operation. Of 44 cases of carcinoma of the small intestine reported by Hinz, 12 cases had no operation at all, 4 cases only an exploratory celiotomy, 12 cases a palliative operation and 16 cases a radical operation. Of the 16 cases subjected to a radical resection, 7 cases died from the operation, 3 died of recurrence and 2 of intercurrent disease without metastases within two years. One was free of recurrence at the end of seven years and two at the end of three years.

Hinz divides the cases in his series into two groups:

those with stenosis and those without stenosis. There were 28 cases with intestinal stenosis, of which 12 cases, or 43 per cent., were subjected to a radical operation. There were 16 cases without intestinal stenosis, of which 4 cases, or 25 per cent., were suitable for radical removal. The study of these two groups would indicate that the cases with intestinal stenosis come earlier to operative treatment. This is probably due to earlier local signs. The late stage at which the cases come to operation probably explains the high operative mortality and the poor end results. The nature of the operation is not one that should be associated with a great risk, and the anatomical relations of the intestine and the nature of the growth, favor better end results. A number of the cases included in the series were operated upon previous to the more modern intestinal technique. This of course greatly influences the results.

Treatment.—The surgical treatment may be radical or palliative. The radical operation consists of the removal of the growth with the neighboring lymphatic glands and joining the intestine either by a lateral or an end-to-end anastomosis. The palliative operation consists of making an anastomosis between two coils of the intestine, leaving the carcinoma out of the course of the intestinal contents.

The medical treatment is to relieve pain with codeine, and when necessary with morphine, to assist the bowels to overcome the obstruction in the intestine, and to treat other symptoms that may arise.

CARCINOMA OF THE LARGE INTESTINE.

Etiology.—*Frequency.*—In the series of 1453 cases of carcinoma of the gastro-intestinal tract reported by Mayo, 215, or about 15 per cent., occurred in the large intestine. That is, carcinoma is much more frequent in the large than in the small intestine, and occurs with about the same frequency in the entire large intestine, including the sigmoid flexure, as it does in the rectum.

Sex.—Of 128 cases of carcinoma of the large intestine reported by Anschütz from the Breslau surgical clinics, there were 91 males and 37 females. Of 39 cases reported by Denk from von Eiselberg's clinic, 23 were males and 16 females. Other observers report a smaller difference in the liability of the sexes to the disease, but all seem to indicate that the condition is more common in males than in females. This agrees with the occurrence of carcinoma in other parts of the gastro-intestinal tract, as reported from various surgical clinics.

As stated elsewhere, Bashford's mortality statistics give malignant growths of the intestines as a more frequent cause of deaths of females than of males. As cancer of the rectum is grouped separately and the small intestine is rarely the seat of a primary malignant growth, his statistics are practically those of the large intestine alone.

Age.—Carcinoma of the large intestine follows the usual rule as to age. Most cases occur after the age of forty years, but it is occasionally observed in early years. Of the 128 cases reported by Anschütz, there were 2 cases between the ages of ten and twenty years, 6 cases between twenty and thirty years, 20 cases between thirty and forty years, and 100 cases over forty years. In Denk's series there were 2 cases between the ages of twenty and thirty years, 2 cases between thirty and forty years, and 35 cases past forty years.

Location.—In the 128 cases reported by Anschütz and the 39 cases reported by Denk the location of the growth was as follows:

	Anschütz's series.	Denk's series.
Cecum	24	11
Ascending colon	10	4
Hepatic flexure	9	3
Transverse colon	15	4
Splenic flexure	17	4
Descending colon	4	1
Sigmoid flexure	49	12
	128	39

The frequency with which the different parts of the large intestine are involved is nearly in the same proportion as each of these series, and follows in the order of the theoretical amount of irritation from the intestinal contents. In the sigmoid flexure, the fecal matter is not only more solid than in the other parts of the large intestine, but it may be actually hard and irritating and it may be retained there for a considerable period of time, much longer than at any other place. At this point there is the greatest amount of irritation to the lining of the intestine from the intestinal contents, and it is also here that the greatest number of cases of carcinoma of the large intestine is found. In contrast to the sigmoid flexure, carcinoma of the large intestine is least frequent in the descending colon, a part which offers little resistance to the onward passage of the intestinal contents and which much of the time is entirely empty. Next to the sigmoid flexure the cecum is the most frequent site in the large intestine for a carcinoma to develop, and it is also a place in which feces are often abnormally retained. Comparing the hepatic and splenic flexures, it is found that carcinoma is more frequent in the latter than in the former locality. The more solid condition of the feces and the more acute angle of the splenic flexure would explain the difference.

Moynihan doubts the accuracy of the belief that carcinoma of the colon is more frequent at the flexures and believes that it rarely occurs at the exact bend of the bowel, but one, two or three inches from it. He states that he has never seen a growth develop exactly at the hepatic flexure and rarely at the splenic flexure.

Trauma.—It is difficult to trace the direct connection between an external injury and a carcinoma of the large intestine. The large intestine is well protected in the abdomen and it is not easily injured. The cases reported as occurring as the result of injury are probably cases in which there was a preëxisting cancer and the injury started or directed attention to the symptoms.

Constipation.—Internal injury to the mucous membrane by hard or irritating feces is a more likely cause of the malignant growth. It has already been stated that carcinoma develops most frequently in those parts of the intestine which are subjected to the greatest irritation.

Ulcers.—It has not been demonstrated that carcinoma develops in an intestinal ulcer as it has that it develops in a gastric ulcer. Intestinal ulcers are not as frequent as gastric ulcers, and would not as often be the cause of the development of a cancer. By analogy to the conditions in the stomach, and by our knowledge that cancer results from continued irritation, particularly of an abnormal lesion, it is probable that an intestinal ulceration or scar may predispose to the formation of a carcinoma of the intestine.

Polypoid Growths.—These are in the same category as intestinal ulcers. Even if originally benign, the constant irritation of the feces may favor the change to a malignant growth in the large intestine, as is more frequently demonstrable in the rectum.

Symptoms.—*Pain.*—This is usually but not invariably present in intestinal carcinoma. It may be an indefinite discomfort over the entire abdomen and become localized only during the late stages. When it is localized it is usually over the growth, but may be in another part of the abdomen. The most characteristic type of pain is the attacks of colic due to the tonic peristaltic action of the bowels above the stricture. This may be started by an attack of indigestion, traumatism or anything causing irritation of the intestine.

Constipation.—This is one of the early and most constant symptoms of intestinal carcinoma. It is progressive and gradually becomes more marked as the disease advances. It may be relieved by attacks of diarrhea during which the intestinal contents, being more fluid, pass through the stricture. It may also be relieved by sloughing of the growth, if the lumen of the intestine is made more patent.

Flatulence.—On account of the retention of the intestinal contents, there is an increased production and a diminished expulsion of gas which causes intestinal distention. This may be extensive and cause a general abdominal distention. More frequently it is limited or most marked in the intestine directly above the growth.

Obstruction.—An absolute intestinal obstruction may be the first symptom of a carcinoma of the large intestine. The obstruction may be caused by a volvulus or an intussusception or a kinking of the intestine. Of 128 cases in the series reported by Anschütz, there were 51 cases, or 40 per cent., of ileus, and of these 50 per cent. died. The following table taken from his article gives the location, the number of cases of ileus, and of deaths:

	Cases.	Ileus.	Deaths.
Cecum	24	6	4
Ascending colon	10	0	0
Hepatic flexure	9	4	3
Transverse colon	15	1	1
Splenic flexure	17	9	6
Descending colon	4	0	0
Sigmoid flexure	49	31	11
	128	51	25

Tumor.—The demonstration of a tumor attached to the colon is a sign of most importance in the diagnosis of carcinoma of the large intestine. A tumor was present in 66, or approximately one-half of the 128 cases in Anschütz's series. The tumor mass may be composed partly of the malignant growth and partly of fecal matter. The size of the tumor varies on different days and is diminished if the bowels are thoroughly emptied by laxatives and the fecal obstruction removed. At times the tumor, which may be felt on some days, entirely disappears on others. The tumor is usually sensitive to pressure.

Increased Peristalsis.—This is a natural symptom to expect with the intestinal stenosis. There is an obstruc-

tion to the passage of the fecal matter through the stricture; the intestine must use more force to get it through. This increased peristalsis may be seen in waves or felt with the hand on the abdomen. The increased peristalsis was noticed in about 43 per cent. of the cases in Anschütz's series. Associated with the increased peristalsis are attacks of colicky pain. These attacks may be relieved by attention to diet and the regulation of the bowels.

Feces.—There is little to be learned from the shape of the movements. They may be small in size or ribbon-shaped if the growth is in the rectum but not if it is above the sigmoid.

The microscopic examination of the feces may give more and definite information. Blood, pus, mucus, and pieces of tissue may be found. The blood may be either visible or occult. Care must be taken to exclude gastric, intestinal, and rectal ulcers, hemorrhoids, fissure, etc. If the presence of the blood is persistent, particularly if associated with pus and mucus, carcinoma of some part of the gastro-intestinal tract should be suspected. Pus is of more significance than mucus, as the latter is often the result of a catarrhal inflammation of the intestine. Pieces of tissue may be found and are of positive diagnostic value. If the growth is in the sigmoid there may be tenesmus.

Perforation.—This may be the result of the necrosis of a portion of the intestine strangulated by the ileus, or it may be the result of the extension of the growth itself. If the perforation is rapid, as in cases associated with ileus, a general septic peritonitis is the immediate result. If it occurs more slowly, adhesions between the intestine and surrounding organs will have formed and a circumscribed abscess, or a fistula between the intestine and some other organ, most frequently the stomach and bladder, or a general peritoneal carcinosis will result. If the communication is formed with the stomach, fecal matter will be found in gastric contents or undigested pieces of food with the movements. If with the bladder, fecal matter

will be passed with the urine. Such conditions will occur only in the late stages of the disease.

Metastases.—It is generally accepted that metastases from a carcinoma of the large intestine occur late. This is a factor in the favorable results obtained by operation on those cases seen in the stage in which a radical operation is possible. It is another indication of the mild degree of malignancy shown by most cases of carcinoma of the large intestine. Metastases occur most frequently in the liver and in the mesenteric lymph nodes. The involvement of the peritoneum is frequent and results from direct extension and peritoneal transplantation of cancer cells.

Prognosis.—Carcinoma in the large intestine shows a milder degree of malignancy than in any other organ, though without operation all cases are ultimately fatal. Without operation the average course of carcinoma of the large intestine is from two to four years. As there are no symptoms in most cases in the early stages, it often is impossible to determine the approximate duration but probably some of the most malignant cases terminate fatally in six months. There are a number of cases that have had an exploratory celiotomy, and concerning the diagnosis of which there can be little doubt, that have lasted over three years. The cases that are said to have lasted five or six or more years are questionable. The probable explanation of these cases is that a malignant process has developed in a preëxisting benign tumor or stricture. It is not likely that a carcinoma of even a mild degree of malignancy could last so long a time.

Treatment.—For the consideration of the treatment, the cases of carcinoma of the large intestine will be divided into two classes, depending on the presence or the absence of complete intestinal obstruction.

In carcinoma of the large intestine with *complete obstruction*, the immediate indication is to relieve the acute condition. This indication is to form an artificial anus or an intestinal anastomosis, but with rare exceptions not to attempt to remove the growth. The general condition

of the patient and the local disturbance in the peritoneum are unfavorable to any extensive operative work. Many of these cases have had previous attacks of obstruction which have been relieved by medical means.

It may be difficult to determine when the attack requires surgical interference. By waiting, if the obstruction is relieved by medical means, any operation will be avoided or done under more favorable conditions, and a single operation instead of two may be sufficient. By waiting too long, strangulation and perforation of the intestine may result, and a general peritonitis develop. The safer plan is to interfere surgically too early rather than too late.

1. The *artificial anus* should be made at the most convenient place above the obstruction. If it is made too near the obstruction, the extension of the growth may interfere with its function and necessitate a subsequent operation. If it is made at too great a distance from the obstruction, there may be retention of discharge in the intervening portion of the intestine which may cause trouble. The operation is a simple one and can be done under local anesthesia if necessary. The deaths following it are usually due to the condition requiring it and not to the operation itself. The most frequent cause of death is general peritonitis, which had started previous to the operation, or which may develop subsequently from perforation of the intestine at the site of the growth or at the point of strangulation. If the condition of the patient will permit, it is best to do the operation in two stages, first suturing the intestine to the abdominal wall, and opening it a few hours later when the intestine has become adherent to the peritoneum.

2. An *intestinal anastomosis* for an obstruction due to a malignant growth is a more ideal operation than an artificial anus, but is associated with a greater risk and is justifiable in few cases. It requires the anastomosis of the intestine above the obstruction, which is distended, to that below the obstruction, which is collapsed. This is technically difficult and associated with an increased risk.

The technical difficulties, the local and general condition of the patient, and the increased time of the operation are all against the intestinal anastomosis and in favor of the artificial anus. An intestinal anastomosis in preference to an artificial anus should never be done excepting under favorable conditions. If the case is seen early, when the general condition of the patient is good, when there is no peritoneal disturbance, and only moderate distention of the intestine above the obstruction, an anastomosis may be indicated. These conditions, unfortunately, do not often obtain.

The location of the growth is a factor in deciding between an anastomosis and an artificial anus. If the growth is situated in the sigmoid flexure and cannot be removed, an artificial anus in the colon is the only relief that can be given to the patient. An artificial anus in the colon does not interfere with the nutrition of the patient, and is relatively easy to care for. If, however, the growth is in the cecum, the artificial anus would have to be in the small intestine. The more fluid condition of the intestinal contents in the small intestine makes such an anus more difficult to care for and more disagreeable to the patient. This fact, together with the possible interference with nutrition, would make a subsequent anastomosis desirable even if the growth could not be radically removed.

That is, the advantage to be gained by the immediate anastomosis is obtained only when the growth is situated in the upper part of the colon. It is a mistake to seek the advantage at too great risk to the patient, and the cases of obstruction due to an intestinal carcinoma in which an immediate anastomosis is indicated are infrequent.

3. The *radical removal* of a carcinoma of the large intestine during an obstruction is the ideal operation but it is not frequently possible. The resection of the intestine, that is, the removal of the growth and anastomosis of divided intestine, is technically difficult for the reasons already given. It is associated with a mortality estimated

between 50 per cent. and 70 per cent. and is therefore rarely indicated. There are some cases in which the growth is situated in a loop of intestine with a long mesentery, or which can easily be mobilized, that can be treated by drawing the intestinal loop containing the growth outside of the abdomen and fastening it to the abdominal wound. The growth is removed at once or after adhesions have formed, as the case indicates, leaving an artificial anus. In these cases, before the abdomen is closed, the portion of intestine leading to the growth and that leading from it are brought together laterally forming a spur in the artificial anus. This spur is later divided by the application of a clamp and the anus closed. The objection is raised to this method that it is applicable only to cases favorable to a radical operation, and in such cases if an artificial anus is first made and the removal of the growth left for a subsequent operation under more favorable circumstances, a more radical operation with greater attention to the removal of lymphatic glands can be performed, giving a greater chance for a permanent cure.

For carcinoma of the large intestine without acute obstruction there are also three operative procedures. They are:

1. Radical removal.
2. Intestinal anastomosis without removal.
3. Artificial anus without removal.

1. The *radical removal* of a carcinoma of the large intestine is the only operation that will cure the patient and all other operations are merely to relieve symptoms. In properly selected cases, the operative mortality is becoming constantly lower and the end results more favorable. With carcinoma of the large intestine as in other organs, a lower operative mortality and a higher percentage of permanent cures are to be obtained by earlier diagnoses. The operative risk of the removal of an early growth in the large intestine is no greater than of the removal of malignant growths from other abdominal organs and on

account of late metastases and the nature of the growth itself, the end results are probably more favorable than those following the removal of malignant growths from any other organ.

The radical removal of a carcinoma of the large intestine may be accomplished in a one-stage or a two-stage operation. The one-stage operation is usually performed for all malignant growths in the first half of the colon or as far as the splenic flexure, because the movable ileum can easily be anastomosed to the transverse colon and for favorable cases beyond the splenic flexure. For a growth in the lower half of the colon, particularly in the sigmoid flexure, and in advanced cases, the two-stage operation is more often selected, as an anastomosis between two parts of the large intestine is more difficult.

The *one-stage operation* is the ideal operation but it is associated with a higher primary mortality. In it the growth is removed and the intestine immediately reunited either by an end-to-end or a lateral anastomosis. A liberal portion of apparently healthy intestine is removed on each side of the growth to be sure that all malignant tissue in the intestine is removed. Metastases appear late, but all lymphatic glands along the course of the vessels should be removed. If the growth is in the cecum, about four inches of the ileum, the cecum, appendix, ascending colon, hepatic flexure, and a part of the transverse colon are removed and the ileum anastomosed to the transverse colon, that is, an ileocolostomy is made. The amount of colon removed is partly to extirpate the disease widely and partly to permit the more easy anastomosis between the ileum and the transverse colon. The same operation is done if the growth involves the ascending colon or hepatic flexure, except that a larger portion of the transverse colon is removed. If the growth is in the transverse colon it may be removed and the colon directly reunited either by end-to-end or the lateral method. The transverse colon is usually sufficiently looped downward to allow easy access to it and room for the direct anastomosis

after the growth has been removed. Carcinoma of the splenic flexure and of the descending colon may also be treated by removal and immediate anastomosis. After a removal of a carcinoma of the sigmoid flexure the ends of the intestine should be anastomosed if possible. In some cases this is not possible and a permanent colostomy may be necessary.

In the *two-stage operation* the loop of colon containing the carcinoma is "mobilized," that is, it is freed of its peritoneal attachments, until the growth with a liberal amount, that is, three or four inches, of normal intestine on either side of it can be withdrawn and fastened outside of the abdominal wall. Before closing the abdomen the two pieces of intestine, the one leading to the growth and the one leading from it, are sutured together laterally. After adhesions between the intestinal loop and the parietal peritoneum have formed, the growth is cut away. By this procedure the danger of peritoneal infection from intestinal contents is avoided. Later, usually at the end of about three weeks, the spur is removed by the application of a clamp and the artificial anus is closed.

2. An intestinal anastomosis without removal for carcinoma of the large intestine is, of course, not curative, and is made to relieve pain or chronic obstruction in cases otherwise inoperable. It has obvious advantages over an artificial anus, though associated with a slightly increased operative risk. The simplest method is to anastomose laterally the intestine above the growth to some portion below it. The intestinal contents are thus side-tracked around the stricture, and the obstruction and pain are relieved. When anastomosed in this way, there is a tendency for the intestinal contents to pass along the colon in the normal track instead of passing through the new opening, and to keep up the pain and irritation of the growth. To avoid this in some cases, the loop of intestine containing the growth is entirely severed at the proximal or oral side so that none of the intestinal contents pass into the loop containing the growth but are side-tracked

around it by means of an end-to-side or lateral anastomosis. The treatment of the loop which has been excluded is varied. Formerly the ends were turned in, sutured, and returned to the abdomen without drainage. By this method, there was no outlet for the intestinal secretions and discharges from the growth, and trouble resulted. It is therefore necessary to drain this excluded intestinal loop. This is usually done by forming an external fistula sometimes by an anastomosis to the sigmoid flexure.

3. An *artificial anus* is rarely made for a growth in the intestine in the absence of an acute obstruction. There are some inoperable cases, situated too low in the colon or sigmoid to permit an anastomosis, in which an artificial anus is necessary to relieve the chronic obstruction and pain. If the growth is higher in the colon, even if otherwise inoperable, an anastomosis around it is possible and a more satisfactory result obtained.

Operative Mortality.—This is not easy to state in definite figures for as much depends on the condition of the patient and on the local condition as the operation. The cases with ileus should be separated from those without symptoms of acute obstruction.

With an *acute obstruction* an intestinal resection is associated with a mortality estimated as high as 75 per cent. and on account of the high risk is rarely done. This mortality rate is considerably lessened, even during ileus, by the two-stage operation in which the growth is drawn outside of the abdomen and an artificial anus made. The formation of an artificial anus is associated with the least risk of all the operative procedure for the relief of an obstruction due to a carcinoma of the intestine.

Without an acute obstruction the danger of an intestinal resection is distinctly less and depends on the extent and location of the malignant growth.

Anschütz, in a series of cases of primary intestinal resection for carcinoma of the large intestine, collected from various authors and from which all cases of ileus were excluded, reported an operative mortality of 46

per cent. This percentage is, however, misleading, as many of these cases were operated upon previous to the development of modern intestinal surgery. Mayo, in 1909, reported eight deaths or 13 per cent. in 61 cases of resection for carcinoma of the large intestine. The low rate for primary resection of the colon for carcinoma can only be obtained by doing a resection on cases suitable for it. The two-stage operation for a certain class of cases has lowered the mortality from primary resections. Anschütz in the same article in which he reported a mortality rate of 46 per cent. for primary resection, reported only 12.5 per cent. operative mortality for the two-stage operation. The two-stage operation has been a distinct advance in the surgery of the large intestine.

End Results.—An artificial anus and an intestinal anastomosis around the growth are only palliative operations and ultimately the disease terminates fatally. The palliative operation has not only relieved symptoms but doubtless prolonged life. The average duration of life after the formation of an artificial anus, according to Anschütz, is approximately one and a half years. This is a very favorable result when it is remembered that these operations are performed only on cases otherwise inoperable.

The end results of the radical operation for carcinoma of the large intestine are very favorable. If only cases that are operated upon according to modern ideas of the surgery of the large intestine are considered, and cases previous to ten years ago are excluded, probably 50 per cent. of the cases that recover from the operation are free of recurrence at the end of five years. The results of the removal of malignant growths of the large intestine by modern methods are probably more favorable than the removal of such growths from any other abdominal organ.

SARCOMA OF THE INTESTINES.

Etiology.—*Frequency.*—Sarcoma of the intestines is a rare disease. Only 1 or 2 per cent. of the cases of malig-

nant disease of the intestines are sarcomata. Unlike carcinoma, sarcoma occurs with the same or greater frequency in the small than in the large intestine, and in the small intestine it occurs with nearly equal frequency in each of the three parts.

Sex.—Sarcoma of the intestines occurs somewhat more frequently in males than in females. In a series of 22 cases of sarcoma of the large intestine reported by Jopson and White there were 12 males and 10 females. In 101 cases, Speese reports 67 cases were in males and 34 in females.

Age.—The following table gives the age of a series of 51 cases of sarcoma of the small intestine collected by Libman and of a series of 22 cases of sarcoma of the large intestine collected by Jopson and White:

Age.	Small intestine.	Large intestine.	Total.
Under 10 years	6	7	13
10 to 20 "	9	3	12
20 to 30 "	13	4	17
30 to 40 "	13	5	18
40 to 50 "	8	1	9
50 to 60 "	1	1	2
Over 60 "	1	1	2
	51	22	73

The early age, especially when compared with carcinoma of the intestine, is noticeable. Of the total number of cases in the two series, 18 per cent were under ten years of age and 70 per cent. were under thirty years of age. One case of sarcoma of the small intestine was congenital.

Pathology.—Sarcoma of the intestine may begin in the lymphoid tissue in the intestinal wall or in the connective tissue. The lymphosarcoma and the small round-cell variety are the most common types and constituted 77 cases in a series of 99 cases. The growth is usually single, and involves only a limited portion of the intestine, but it may be multiple or it may involve a large part of the intestinal tract. The tendency of the growth is to spread in the submucus and muscular coats, but later may

penetrate the serous layer and involve neighboring coils of intestine by direct extension. On account of the weakening of these coats, possibly also by interference with the nerve supply, there is a distention of the intestine. The distention may involve a part of the circumference of the intestine giving rise to a globular swelling on one side, or more rarely it may involve the entire circumference of the intestine producing a fusiform swelling. In a few instances the sarcoma has been found to grow toward the lumen of the intestine, producing an obstruction by the size of the tumor but not usually by the formation of a stricture as is frequent with carcinoma of the intestine. In a few cases in which fibrous tissue predominated, a true stricture has been found. The tendency of sarcoma of the intestine, especially of lymphosarcoma and of round-cell sarcoma, is to spread to the neighboring lymph glands in the mesentery. These metastases are formed early in the disease. Later the abdominal organs, particularly the liver, are involved with metastatic deposits.

The tendency of a sarcoma of the intestine to produce a distention of the bowel is characteristically different than carcinoma which tends to cause a stricture, and is the cause of marked difference in the symptoms of the two diseases. In carcinoma of the intestine, the first symptoms are those due to the increasing obstruction to the intestinal contents. In sarcoma there is usually distention instead of stricture of the intestine and there are no early local symptoms as in carcinoma.

Symptoms.—*General.*—In sarcoma of the intestine, the early symptoms are the constitutional symptoms of a malignant growth without the local signs. The patient becomes anemic and there is marked loss of flesh and strength. There may be nausea and vomiting and a general disturbance in the gastro-intestinal tract without definite local symptoms.

Pain.—This is not an early symptom of the disease. There is more general abdominal discomfort than actual pain. Later the abdomen may be distinctly tender.

Bowels.—Constipation may result from lessened nerve and muscle power or more rarely by the extension of the tumor toward the lumen of the intestine or by the formation of a true stricture. Constipation as a symptom of intestinal sarcoma is mentioned more frequently in cases recently reported than formerly. Complete obstruction from kinking or intussusception has been reported in a number of cases.

Abdominal Distention.—In addition to the enlargement of the bowel at the site of the tumor, there may be a general abdominal distention due to the constipation and accumulation of gas, or to the peritoneal involvement or to the pressure on vessels by extension of the growth. The abdominal distention may come on suddenly and resemble tuberculous peritonitis.

Tumor.—Late in the course of the disease, a tumor may be palpated. The tumor is usually not tender and moderately movable. If limited to a single coil of intestine, it may feel smooth, soft, and cystic. If other coils of intestine are involved by extension, it is a more hard, irregular, indefinite and less movable mass.

Feces.—Blood, either visible or occult, may be found in the feces, especially if the growth is in the large intestine. Sloughing of the growth does not occur as regularly as it does with carcinoma but it may happen and the feces may contain pus and pieces of tissue.

In a case reported by Bjorkenheim, a sarcoma of the intestine was diagnosed as an ovarian cyst. This mistake has been noted by other observers. As the sarcoma frequently occurs in the small intestine which is movable, it gravitates to the pelvis. A tumor in that locality with a cystic feeling in a female would easily be diagnosed as an ovarian cyst.

Prognosis.—This is always bad and there are few cases on record of a sarcoma of the intestine being cured even by surgical interference. The absence of early local symptoms prevents a diagnosis and an operation, at a stage of the disease during which a permanent cure would be

likely. Most cases die within the first year and rarely does a case last over eighteen months after the appearance of the first symptoms.

Treatment.—The surgical removal of the growth offers the only hope of a permanent cure and should be done when possible. A case of sarcoma of the intestine is rarely diagnosed previous to operation, and most cases on which an operation has been performed were incorrectly diagnosed or discovered only by an exploratory celiotomy. If by direct inspection, it seems probable that the growth can be removed, a resection would be indicated. As many of these cases are in the small intestine, and symptoms of obstruction are not usually present, neither an artificial anus, nor an intestinal anastomosis without removal of the growth, would often be indicated, as in carcinoma of the intestine. Medical treatment would be directed to alleviating symptoms.

CARCINOMA OF THE APPENDIX.

Etiology.—*Frequency.*—In a total of 8039 specimens from the Mayo Clinic, MacCarty and McGrath reported 40 cases, or 5 per cent., of carcinoma of the appendix. In 5 cases only were there gross changes which suggested carcinoma. In the remaining 35 cases the carcinoma was discovered at the routine examination in the pathological laboratory. In a total of 6505 appendices from a number of operators there were, as reported by McWilliams, 26 cancer, or about 0.4 per cent. In this series, however, probably all the appendices removed were not examined, and doubtless more cases would have been found if a routine examination of all specimens removed had been made.

In a number of instances a carcinoma was found in an appendix which was removed at an operation for some pelvic lesion with no suspicion that the appendix itself was diseased. This is in favor of removing the appendix,

if it is easily accessible and the patient is in good condition, during operations for other abdominal lesions.

Age.—In the series of MacCarty and McGrath one case, a female, occurred at five years and two cases, one a male, the other a female, at ten years of age. The average age of all the cases was thirty years. It is of interest that the child of five years with the carcinoma of the appendix had had symptoms since her birth.

In the series reported by McWilliams and that of Rolleston, a total of 78 cases, there were 2 cases under ten years of age and 16 between the ages of ten and twenty years. The average age of these 78 cases was 27.7 years. McWilliams has called attention to the early average age of cases of carcinoma of the appendix, compared with that of other parts of the intestinal tract, and that the age of cancer of the appendix coincides with that of appendicitis. This is of value in considering the influences of chronic inflammation of the appendix as a cause for the development of carcinoma of the appendix.

Sex.—Of 37 cases in the series of MacCarty and McGrath with complete records, there were 26, or 70 per cent., females and 11, or 30 per cent., males. In the combined statistics of McWilliams and Rolleston there were 44, or 57 per cent., females and 33, or 43 per cent., males. In all other parts of the gastro-intestinal tract, carcinoma is probably more frequent in males than in females. A possible explanation of the greater number of cases of carcinoma of the appendix in females is the greater number of abdominal operations performed in women and the removal of the appendix even though it is not apparently diseased. Chronic appendicitis may be more common in men, but more women have their appendices removed, and possibly for this reason more cases of carcinoma are found.

Concretions.—In the series of 90 cases reported by McWilliams there were only 5 cases in which a concretion and one other case in which a fish-bone was found. Concretions were found less frequently than in chronic

appendicitis. This is in contrast to carcinoma of the gall-bladder which is frequently associated with gall-stones and which are believed to favor the development of carcinoma in that organ. A possible explanation is the difference of real irritation in the two conditions. Gall-stones are hard and the gall-bladder is frequently changing in size so that there is definite irritation to its lining. It is the constant, frequently repeated irritation that is a factor in the development of a carcinoma. The concretion in an appendix in reality is soft and smooth and is the source of little irritation.

Pathology.—McWilliams gives the following classification of the carcinomata of the appendix, and the frequency of occurrence of the different types:

Spheroidal-cell carcinoma	53.5 per cent.
Columnar-cell carcinoma	22.5 "
Transitional	9.8 "
Mixed	5.6 "
Colloid	4.2 "
Endotheliomata	4.2 "
	99.8 "

Metastases. — In McWilliams' series, carcinomatous glands were demonstrated microscopically in only 1 case. There were enlarged glands in 8 cases, but in 4 cases they were not malignant, and in 3 cases no microscopic examination was made. Metastases in other organs practically are never seen.

Extension of the Growth.—Carcinoma of the appendix long remains a local disease. Microscopically it may extend through the various layers of the appendix and on to the mesentery, and from this extension, the neighboring intestines and peritoneum may be involved. The growth may extend to the cecum, and it is probable that some cases considered to be primary in the cecum really began in the appendix. Even if the growth has apparently spread from the appendix to the cecum, it may continue its benign course. One case reported

by McWilliams was considered at the first operation to be an inoperable malignant growth in the intestine and the abdomen closed. Twenty months later the abdomen was reopened, the appendix and some glands were removed for examination. The appendix contained a spheroidal-celled carcinoma but the glands showed no signs of malignant disease. Nine years later this patient was alive and in perfect health. The case illustrates the benign clinical course of carcinoma of the appendix.

Situation of the Tumor.—In the series of MacCarty and McGrath the growth was situated at or near the tip of the appendix in over 90 per cent. of the cases. In the series of McWilliams, it was situated at or near the tip in 59 per cent., in the middle in 14 per cent., near the base in 14 per cent. of the cases. It was situated distal to the middle of the appendix in 76 per cent. and proximal to the middle in 15 per cent., and involved nearly the whole of the appendix in 8 per cent. of the cases. That is, the growth occurs usually in the outer half of the appendix. There seem to be a direct relationship between the location of the carcinoma and the site of a stricture or obliteration of the lumen.

In 5000 cases reported by MacCarty and McGrath, carcinoma of the appendix was found in 1.6 per cent. of the cases in which there was a complete or partial obliteration of the lumen. It is probable that this cicatricial change in the appendix is an etiological factor in the development of a carcinoma.

Duration of Symptoms.—Of the cases in the series of MacCarty and McGrath, the duration of symptoms was one year or less in 11 cases, one to two years in 4 cases, two to three years in 2 cases, three to four years in 5 cases, and four or more in 14 cases. One case of five years of age had had symptoms since birth. These statistics cannot be interpreted to mean that carcinoma existed in the appendix for the periods given before it was removed. Previous to the development of the car-

cinoma there probably existed a chronic appendicitis which was the cause of the early symptoms.

Symptoms.—In the *early stage* the symptoms of carcinoma of the appendix are the symptoms of chronic appendicitis, with recurring acute attacks. The diagnosis is never made previous to operation and rarely even at the operation but the condition is found in the laboratory by routine examination of all appendices removed.

In the *late stage*, the symptoms resemble those of carcinoma of the cecum, but probably without signs of obstruction. A tumor may be palpated in the right iliac region. Such a tumor may be composed of the primary tumor in the appendix with its extension to the cecum, and the small intestine adherent to it, the whole forming an irregular and indefinite mass. The tumor may be an abscess resulting from the perforation of the appendix by extension of the growth.

Prognosis.—This is so favorable that carcinoma of the appendix is clinically an early benign tumor. McWilliams reports only one case that was known to have recurred. The operative risk is that of appendicitis, for which the operation was performed, and it is not changed by the carcinoma.

Treatment.—This is, of course, the surgical removal of the appendix. As has been stated, this is usually done for appendicitis without the diagnosis of carcinoma having been made. If a carcinoma were suspected, the mesentery should be divided at a distance from the appendix. If the growth involves the base of the appendix, a piece of the cecum should be removed.

CANCER OF THE RECTUM.

Etiology.—*Frequency.*—In Bashford's mortality statistics, primary malignant growth of the rectum was the cause of 7 per cent. of a total of 84,448 cancer deaths. Clogg states that about 3 per cent. of primary cancers occur in the rectum. In one series of cases reported

by Mayo, carcinoma was found with practically the same frequency in the rectum as in the large intestine.

Age.—As in cancer in other parts of the body, carcinoma of the rectum is most frequently a disease of middle and advanced age. Seventy per cent. of the cases are between the ages of forty and seventy years; 50 per cent. of the cases are between the ages of fifty and sixty-five years. More frequently than in other organs, carcinoma of the rectum occurs in early years. For example, Kammerer reported a case of carcinoma of the rectum in a child of six months. Grulee records an adenocarcinoma of the rectum in a girl, aged sixteen years, and refers to other younger cases in the literature. A possible explanation of the frequency of carcinoma of the rectum in early life is the occurrence of papilloma of the rectum in children and its conversion into carcinoma.

Sex.—Carcinoma of the rectum occurs more frequently in males than in females. Some surgeons give the proportion of two to one. This ratio, however, is probably too high. In Bashford's mortality statistics, there were about 15 per cent. more deaths from cancer of the rectum in males than in females. This is not as would be expected from the etiology, as ulcers, hemorrhoids and constipation, which are considered possible causes of carcinoma of the rectum are decidedly more frequent in women than in men.

The knowledge of the real cause of carcinoma of the rectum is as indefinite as that of the cause of carcinoma in other parts of the body. There are, however, certain conditions and lesions which apparently are factors in the causation of cancer of the rectum.

Rectal Polypi.—There seems to be no doubt that rectal polypi have an influence in the development of carcinoma of the rectum. Either as a result of a carcinomatous degeneration of the polypus, or the engraftment of the carcinoma on the polypus, the benign growth is replaced by the malignant cancer. If, as is generally believed, a chronic, constantly repeated irritation or injury

is a causative factor in the production of cancer, it is easy to accept that a rectal polypus may become a recta carcinoma. The polypus is under constant irritation both from the contraction of the bowel pulling on its pedicle, and from the passage of fecal matter through the rectum, and its change from a benign to a malignant condition is possibly the direct result.

Rectal Ulcer.—This is another factor in the production of a carcinoma of the rectum. A chronic ulcer in any part of the body, particularly in the alimentary canal, may change and become malignant. The situation in the rectum where it is constantly irritated by the contraction of the bowel and the fecal matter probably favors the change.

Stricture.—A benign stricture of the rectum is a frequent result of a syphilitic infection. Its influence in the development of cancer is probably the same as that of polypi, ulcers, etc. It is a lesion that is predisposed to frequent irritation and injury.

Hemorrhoids.—The connection with either internal or external hemorrhoids is not easy to prove. With many cases of carcinoma of the rectum, particularly if the case is at all advanced, marked hemorrhoids are present. They may have preceded the rectal carcinoma, or they may be the result of it. Furthermore when the great frequency of hemorrhoids and the relative rarity of rectal carcinomata are considered, it must be accepted that the chance of any case of hemorrhoids developing a carcinoma of the rectum is slight. In most cases of hemorrhoids, however, in which there is a little bleeding with each movement of the bowels, and in those cases in which the hemorrhoids protrude through the anus and are constantly rubbed with the clothing, there exists a definite pathological lesion and a constantly repeated irritation—two important factors in the production of cancer. While it is not proved that hemorrhoids predispose to cancer of the rectum, there is certainly the possibility of it.

An important fact in regard to hemorrhoids is the

frequency with which a carcinoma of the rectum is is incorrectly diagnosed as a case of hemorrhoids. Mayo stated that nearly 15 per cent. of cases of carcinoma of the rectum coming for consultation had recently been operated on for supposed hemorrhoids.

Constipation.—The influence of constipation in the production of carcinoma of the rectum is an indirect one. The retention of hard fecal matter in the rectum or its passage through the rectum can produce an irritation and repeated trauma that favor the formation of a carcinoma of the rectum. This is more marked if there is a polyp, ulcer, or stricture present in the rectum.

Pathology.—Sarcoma of the rectum is relatively rare. Tuttle in a series of 100 cases reported only 6 per cent. sarcomata. The more frequent form of malignant tumor of the rectum is the carcinoma, usually of the type of adenocarcinoma. The following table from Tuttle gives the varieties with percentages, in the 100 cases reported in his paper and is a fair average of the frequency of the different types:

Adenocarcinoma	84 per cent.
Colloid carcinoma	2 "
Scirrhus carcinoma	2 "
Malignant papilloma	2 "
Sarcoma	6 "
Epithelioma	4 "
	100 "

The third portion of the rectum, that is, the portion just above the sphincter ani, and sometimes called the anal canal, is an inch to an inch and a half long and is lined with flat or pavement-epithelium. From 4 to 6 per cent. of the cases of cancer of the rectum originate in the anal canal and are epitheliomata. As a rule, epitheliomata are less malignant than adenocarcinomata, but in the rectum they are often more malignant than epitheliomata in other parts of the body.

The *first and second portions* of the rectum extend from

the pelvic brim near the left sacro-iliac articulation to the anal canal. Together they are eight to ten inches long. The first four or five inches of the rectum, the so-called first part, is covered with peritoneum and is attached to the pelvis by the mesorectum. In this portion of the rectum, it is technically possible to remove a wider area of tissue than in the second portion which is practically covered but not surrounded by peritoneum and is attached directly to the sacrum without an intervening mesorectum. The result of removal of a carcinoma of the rectum is therefore more favorable, both as to immediate mortality and ultimate results, if it was situated in the first than if in the second part of the rectum. Both the first and the second portions of the rectum are lined with columnar epithelium and the variety of malignant tumor most commonly found here is adenocarcinoma. It begins most frequently on the anterior wall.

The growth usually commences as a flat, slightly elevated, thickening of the mucous lining of the rectum. During this early stage, as it gives few or no symptoms, it is rarely seen unless discovered by accident. These growths in the rectum have two marked tendencies, one is to early ulceration, the other is to growth around the gut causing stenosis and obstruction.

The three prominent symptoms of carcinoma of the rectum, namely, pain, bloody discharge and obstruction, depend on these characteristics.

In some cases the tumor is distinctly of a polypoid type. It may be the result of a carcinoma developing in a preëxisting polyp of the rectum, or the result of the action of the bowel repeatedly forcing the growth with its basic attachments downward toward the anus as may be done to any mass in the rectum. In some cases, the growth is found outside of the anus.

In addition to extending around the lumen of the gut, carcinomata of the rectum also extend longitudinally so that before death a number of inches of the bowel may be involved. Handley has shown that microscopically

the longitudinal extension of the disease may be as much as six inches above the apparent limits of the growth. This fact is important because of its influence on the operative technique of the removal of the growth.

Besides the circular and longitudinal growth of the disease, it may also, by direct extension involve the surrounding organs, such as the prostate and bladder in the male, and the vagina and uterus in the female. Coils of small intestine may become adherent to the rectum over the growth, and become involved secondarily by direct extension from the primary growth. This is not apt to occur until the disease is well advanced, as it presupposes that the growth has already involved the thickness of the rectal wall.

If the growth is limited to the first and second portions of the rectum, the lymphatic extension is to the sacral glands; if to the third portion, to the inguinal glands. The liver is the most frequent organ involved by metastases.

Symptoms.—*Early.*—Unfortunately many cases give no early symptoms at all and the case is well advanced before the condition is discovered. It is possible for a case of carcinoma of the rectum to have passed the operable stage before giving symptoms that would suggest its presence.

The tendency of a carcinoma of the rectum is to ulcerate early and to extend around the gut producing a stricture. The three most common symptoms of cancer of the rectum, pain, bloody discharge, and increasing constipation, are due to the stricture and ulceration.

Constipation.—The increasing degree of constipation is the important characteristic of this symptom. This is caused by the tightening of the stricture. Stronger cathartics and finally, in some cases, operative interference are necessary to relieve the obstruction. As a rule the increasing constipation is gradual, but sometimes there is an acute intestinal obstruction necessitating immediate relief.

Bloody Discharge.—A constant diarrhea may be associated with the constipation. A small liquid movement, composed of the fluid feces, blood, and mucus, and sometimes pieces of the tumor tissue, may be passed immediately on rising in the morning and at frequent intervals during the day. There may be a constant desire for a movement but with little material to pass.

Pain.—Usually pain is a late symptom and may be absent entirely. When present locally it may be the result of hard fecal matter being forced through the stenosis of the gut; it may be due to the involvement of the anus in the growth and late in the course of the disease it may be due to the extension of the growth outside of the rectum to the surrounding tissues. General abdominal pain may result from the obstinate constipation.

Rectal Tenesmus.—This is a frequent and distressing symptom. It may be due to the irritation about the anus by the frequent movements, or it may be due to the involvement of the anus by the growth.

Cachexia.—The general health of the patient usually remains unaffected until late in the disease. The patient is able to take and retain nourishment and there is no early loss of weight. Later, on account of increasing constipation, the absorption from the growth and possibly the formation of metastases, there is loss of appetite, failure of the general health, emaciation and weakness, that is, cachexia of a malignant disease.

Duration.—The course of the disease is relatively slow. Some cases, particularly those of the scirrhus type, last three to five years. The medullary type is more rapid and usually terminates under two years. In young patients the growth is more rapid than in those of advanced years.

Diagnosis.—The finger and the proctoscope are important means for the diagnosis of carcinoma of the rectum. If the growth is within reach of the fingers, its characteristic feeling will establish the diagnosis. It is often

possible to remove a piece of the growth to confirm microscopically the findings of the examining finger.

The proctoscope or the sigmoidoscope is a valuable aid in the diagnosis of growths situated higher in the rectum. In addition to the direct vision of the tumor, a piece may be removed with long forceps for microscopic examination.

The rule to make a digital examination of the rectum of all cases giving abdominal or pelvic symptoms, enabled the Mayos to discover five early cases of carcinoma of the rectum before they were sufficiently advanced to give symptoms, and is a good rule to follow.

Treatment.—The treatment of cancer of the rectum will be considered under three headings—the precancerous lesion, the operable cases, and the inoperable cases.

1. *Precancerous Lesions.*—The treatment of the precancerous lesions is the prophylaxis of cancer of the rectum. Any lesion or any condition that may possibly have an influence on the formation of a malignant growth in the rectum should be remedied. The rectal polypi, ulcerations, strictures and hemorrhoids are subject to repeated trauma and should be cured or watched for the first sign of an early malignant growth. By the removal of these lesions the chance of the development of a rectal cancer is lessened.

2. *Operable Cases.*—The treatment of an operable case of cancer of the rectum is its removal by surgical means in a thorough manner at the earliest moment possible. The operability of a case is determined, not alone by the limits of the growth in the rectum, but by the extent of the involvement of the surrounding tissue, the condition of the lymphatic glands, and by the presence of metastases. Mayo states that he has not seen a case of rectal carcinoma, locally removable, which was inoperable on account of the involvement of the lymph nodes, though a number of such cases, however, were inoperable on account of a metastatic deposit in the liver. If the rectum is not movable, but is fixed by the extension of the growth to the tissues fastening

it to the pelvis or to the viscera situated anterior to it, the case should not be considered an operable case and no attempt should be made to remove the growth. The operability of a case may sometimes be determined by a simple examination without an anesthetic. The doubtful case, however, should have the benefit of a thorough examination under an anesthetic and an exploratory incision if necessary.

The following table from Tuttle shows the duration of symptoms previous to operation in his series of 100 operable cases. It also shows the increased operative risk that is associated with the longer duration of symptoms:

		Mortality from operation.
Under 3 months . .	17 per cent.	21.4 per cent.
3 to 6 " . .	16 "	6.6 "
6 to 9 " . .	8 "	14.3 "
9 to 12 " . .	15 "	15.4 "
Over 12 " . .	44 "	22.2 "

It will be noticed that the second highest operative mortality is in the group of cases in which the duration of symptoms was less than three months. Tuttle believed that this group was composed of cases of marked malignancy and in a short time the extent of the growth was so large that an extensive operation was necessary. Mayo states that a number of his cases were operable two years after the first symptoms were noticed.

For the operable case, that is, the case in which the growth is to be removed, there are four types of operation. They are the perineal, the sacral, the abdominal and the combined abdominal and perineal.

The *perineal operation* is indicated in cases of carcinoma of the rectum limited to the anal canal, and in some cases not suitable for an abdominal operation, though the growth is situated higher in the rectum.

In the *sacral operation,* of which the Kraske is an example, the rectum is reached posteriorly by the removal of the coccyx and a part of the sacrum. This approach is also selected for cases not suitable for an abdominal

operation and gives a more extensive exposure of the rectum than the perineal operation. A preliminary colostomy may be done.

In the *abdominal* or *combined abdominal* and *perineal operation*, the growth is approached through an abdominal incision, and may be completed either through this incision or through the perineal route. After the removal of the growth, the divided proximal end of the sigmoid may be anastomosed directly to the rectum, or it may be drawn down to the anus, or it may be drawn out in the inguinal region as a permanent colostomy.

End Results.—The *operative mortality* of recent operations, if all cases are included, is from 15 to 20 per cent. In 27 perineal and sacral operations, Mayo reports 7 per cent. primary mortality, and in 44 abdominal and combined abdominal and perineal operations 20 per cent. primary mortality. Infection is the most frequent cause of death following operation.

In regard to the ultimate results of the operative treatment of carcinoma of the rectum, it may be stated that the higher in the rectum the growth is situated, the better is the prognosis for a permanent cure. When situated in the anal canal, the removal of a cancer is associated with a small operative risk but on account of the anatomical relations of the part, the risk of early recurrence is great. If situated high in the rectum, the risk of removal of a cancer is high, but it is technically possible to remove the growth more widely and the percentage of permanent cures is greater.

3. *Inoperable Cases.*—The treatment of inoperable cancer of the rectum is the treatment of its symptoms. The local treatment of the tumor is only of temporary benefit, but it may relieve symptoms for a time. It has been suggested that the *obstruction* in the bowel by the growth may be relieved by curetting or cauterization. This would certainly be associated with the risk of penetrating the bowel and also of spreading the cancer cells to the surrounding tissues.

The treatment of the *constipation* is both by laxatives and enemata. The laxatives used should be mild and changed frequently so that the bowel does not establish a tolerance for any one. The enemata should be given carefully with a soft rectal tube to avoid injury to the bowel. An enema of a bland oil or of ox gall, retained long enough to soften the fecal matter, facilitates its passage through the stricture. The *diarrhea* may be treated by rectal irrigations.

The *pain* which is caused by the constipation is treated by the attention given to the constipation. The pain caused by the extension of the disease involving other structures, necessitates sedatives and anodynes in increasing doses. In the earlier stages aspirin, heroin, and codein, either separately or in combination, will be sufficient to relieve the suffering. Later in the course of the disease morphin will be necessary. It should be remembered that a cancer of the rectum, even after it is in an inoperable stage, may continue for some months, and the use of morphin should be reserved as far as possible for its terminal stage. At this stage it should be used in sufficient doses to make the patient comfortable.

If the *rectal tenesmus* is due to irritation from the discharge and the frequent movements, the condition may be helped by gently washing the bowel with warm water and by the injection of a bland oil. The application of heat or of ice will often relieve the condition. If the rectal tenesmus is due to the involvement of the sphincter ani it may ultimately be relieved by the destruction of the action of the muscle by the advancement of the disease.

A colostomy is more effectual in relieving the symptoms of cancer but its mental effect on the patient is such that it should not be performed until necessary. It should not be postponed too long. It should be located in the inguinal region as it is there most easily cared for. It should be located sufficiently high in the colon not to become involved in subsequent extension of the

growth and also to prevent prolapse of the intestine. It will give the patient great relief from distressing symptoms and much less discomfort than is at first feared.

LITERATURE.

Baltzer. Arch. f. klin. Chir., xliv, 717.
Bjorkenheim. Zeit. f. Gyn., xxxvi, 1329.
Brill. Amer. Jour. Med. Sci., vol. cxxvii.
Cheney. Amer. Jour. Med. Sci., vol. cxxxix.
Clogg. Choyce, System of Surgery.
Cope. British Med. Jour., 1912, p. 753.
Grulee. Surgery, Gynecology and Obstetrics, ii, 678.
Handley. Lancet, 1911, p. 230 (?).
Harte. Annals of Surgery, vol. xlvii.
Jopson and White. Amer. Jour. Med. Sci., December, 1901.
Kasemeyer. Deut. Zeit. Chir., cxviii, 205.
Lecene. Thèse de Paris, 1904.
Libman. Amer. Jour. Med. Sci., cxx and cxxix, 813.
McWilliams. Amer. Jour. Med. Sci., vol. cxxxv.
MacCarty and McGrath. Annals of Surgery, 1914.
Mayo. Annals of Surgery. Collected Papers, Mayo Clinic.
Mayo. Collected Papers, Mayo Clinic, 1911, 1912.
Moynihan. Cavendish Lecture, 1913.
Powers. New York Medical Journal, January, 1911.
Speese. Annals of Surgery, lxix, 729.
Tuttle. New York Medical Journal, 1908.

CHAPTER XI.

CARCINOMA OF THE GALL-BLADDER AND DUCTS. CARCINOMA OF THE LIVER, CARCINOMA OF THE PANCREAS.

CARCINOMA OF THE GALL-BLADDER AND DUCTS.

Carcinoma of the gall-bladder and ducts maybe primary or secondary. When secondary it is usually a part of a general abdominal carcinosis, sometimes an extension from one of the neighboring organs. Most frequently these organs from which the carcinoma has extended are the liver, stomach, pancreas, and duodenum. In many cases at autopsy it is not possible to determine in which organ the primary lesion existed, and an analysis of early symptoms is a better indication of its location than the direct examination.

Primary carcinoma of the gall-bladder and ducts may occur in any of four different places:

1. The gall-bladder and cystic duct.
2. The hepatic duct.
3. The common bile duct.
4. The papilla of Vater.

Frequency.—Carcinoma of the gall-bladder itself is more frequently seen than that of the ducts. Of the ducts, the common bile duct is most frequently involved.

At the Mayo Clinic, in about 4000 operations on the gall-bladder and biliary ducts, about 2.25 per cent. were for malignant conditions. This, however, probably does not indicate correctly the relative frequency of malignant disease of the gall-bladder and ducts. Relatively more cases of malignant disease of the gall-bladder and ducts

have passed the operable stage before coming under proper surgical care than of other conditions in these organs.

In Musser's series there were 100 cases of carcinoma of the gall-bladder and 18 cases of carcinoma of the biliary ducts. This probably gives the relative frequency with which the gall-bladder and its ducts are involved.

Williams considered that carcinoma of the gall-bladder is exceedingly rare. As evidence of its rarity, he states that among 7297 cancer patients in large London hospitals, he found only 11 cases of primary carcinoma of the gall-bladder. He also quotes Guilt, who found only 5 cases among 11,131 cancer patients in the Vienna hospitals, and Peiche, who, from mortality statistics of Hamburg, found 48 cases among 12,484 cancer deaths. It is hardly possible that these figures even approximately indicate the frequency of the occurrence of carcinoma of the gall-bladder. The natural explanation of them is that the early cases are not diagnosed clinically, and in the late cases the location of the primary lesion cannot be determined.

In Bashford's mortality statistics, malignant growths of the liver and of the gall-bladder are grouped together. Among 84,488 cancer deaths there were 11,531 recorded cases, or 13.6 per cent. of malignant growths of the liver and gall-bladder. This percentage of malignant growths of the liver and gall-bladder is undoubtedly too high, and probably a number of secondary growths in the liver were included. Secondary malignant growths in the liver are frequent; they are easily diagnosed, and easily obscure a less prominent primary lesion.

Age.—The average age of primary carcinoma of the gall-bladder is later than that of most carcinomata; the largest number occur between fifty and seventy years of age.

In Fütterer's series the youngest case was twenty-five and the oldest ninety years of age.

The following table gives the ages in 247 cases of carcinoma of the gall-bladder in Fütterer's series.

Age.	Number of cases.
20 to 29 years	5
30 to 39 "	20
40 to 49 "	44
50 to 59 "	69
60 to 69 "	67
70 to 79 "	37
80 to 89 "	4
90 "	1
	247

Five-eighths of Rolleston's 83 cases of primary carcinoma of the biliary ducts were more than fifty years of age. One case of Musser's series was under ten years of age.

Sex.—Carcinoma of the gall-bladder occurs more frequently in women than in men. In Musser's and in Fütterer's series there were three or four times as many cases in women as in men. This proportion is of interest when it is remembered that gall-stones occur much more frequently in women than in men, and that they are probably the most important factor in the causation of carcinoma of the gall-bladder.

Carcinoma of the biliary ducts differing from carcinoma of the gall-bladder is more frequent in men than in women. For example, Miodowski in 40 cases of carcinoma of the common bile duct collected from the literature found that 26 cases were men and 14 cases women. He also states that Schultze found in 17 cases of carcinoma of the hepatic duct there were 12 cases in men and 5 cases in women. In 85 cases of malignant disease of the biliary ducts reported by Rolleston there were 50 males and 35 females.

Gall-stones.—The frequency with which gall-stones are found associated with carcinoma of the gall-bladder, and the evident chronic irritation and inflammation that are associated with them, leaves little to be desired for positive proof, that the carcinoma of the gall-bladder is the direct result of the gall-stones. This connection between the two conditions is universally accepted. Carcinoma of the gall-bladder resulting from gall-stones

is one of the best examples of a malignant disease resulting from chronic irritation.

Fütterer in 209 cases of carcinoma of the gall-bladder, found gall-stones in 75 per cent.; Musser in 69 per cent.

The fact that carcinoma of the gall-bladder occurs most frequently at its fundus, which is its lowest part, and therefore the point most likely to be irritated by gall-stones, and, secondly, at the beginning of the cystic duct where a gall-stone is apt to become impacted, is additional evidence of the influence of the gall-stones in the causation of carcinoma of the gall-bladder.

Williams does not believe that gall-stones are the cause of cancer of the gall-bladder. It is his belief that cancer of the gall-bladder is a very rare disease, occurring only 11 times in 7297 cancer cases, and that if it were caused by gall-stones it would be found more frequently. As has been stated, it is probable that Williams' figures do not indicate the frequency of carcinoma of the gall-bladder.

It has been suggested that the gall-stones are the result and not the cause of carcinoma of the gall-bladder. Against this, as stated by Wolff, is the fact that in primary carcinoma of the gall-bladder, stones are present in nearly 90 per cent. of the cases, but in only 15, or 16 per cent., of the secondary cases. Additional evidence is the large size or number of gall-stones that are sometimes found with a small malignant growth.

Gall-stones are not present in carcinoma of the biliary ducts in the same frequency as in carcinoma of the gall-bladder. In 67 cases of Rolleston's gall-stones were present in 23 and absent in 44 cases. It is possible that they may have been there but had been passed previous to the examination.

Pathology.—In most cases carcinoma of the gall-bladder is of the columnar variety. Epitheliomata are occasionally seen. For example, Dietz reports 4 cases.

Sarcoma of the gall-bladder is more rare than carcinoma and only a few cases are reported in the literature.

The malignant growths of the biliary ducts are practically all of the columnar-celled variety.

The location of the malignant growth in the biliary ducts in 90 cases is given by Rolleston as follows:

Common bile duct	35
Junction of common bile duct, cystic and hepatic ducts	27
Hepatic duct	22
Cystic duct	6
	90

The growth in the bile ducts is usually small and limited to a part of the duct, and may cause a stricture. In some cases the growth is more diffuse. The obstruction of the biliary duct may be due to the annular stricture or to the filling of the lumen by the growth.

If the growth is in the hepatic duct, it extends early to the liver; if in the cystic duct, to the gall-bladder; and if in the lower end of the common bile duct, to the head of the pancreas or to the duodenum. If the case is not seen early, it may be difficult to determine the primary location.

Though local extensions are common, secondary deposits and metastases are not usually present on account of the rapid course of the disease and its termination before they are formed.

Unless there is present other cause of obstruction, such as an impacted gall-stone, the bile ducts below the growth are normal; above it they are dilated.

Symptoms of Carcinoma of the Gall-bladder.—A previous history of gall-stones is usually present. Most early diagnoses are made only at an operation for gall-stones, as in many cases there are no symptoms that will allow a differential diagnosis to be made between the two conditions.

Pain.—A dull pain referable to the region of the gall-bladder is usually the first symptom. It may be referred to the stomach or to the appendix. The pain may be sharp and stabbing and increased by position and exercise. The pain may be in the form of biliary colic. This may

be due to the presence of gall-stones, which may or may not have given symptoms previous to the development of the carcinoma.

In addition to the pain, there may be distinct tenderness over the gall-bladder due to an inflammatory condition in or about the gall-bladder. Musser found pain in 62 per cent. of the cases in his series.

Tumor.—A tumor below the liver is present in 50 to 75 per cent. of the cases, depending on the stage of the disease at which the case is examined. If not adherent to surrounding structures the tumor moves with the diaphragm and possibly also from side to side. In the early stages the tumor is smooth and elastic, but later it is hard and nodular. This may be a diagnostic point of value between primary malignant disease of the gall-bladder and that of the biliary ducts. It may become adherent to the abdominal wall and become immovable. The tumor is usually in the right hypochondrium, but it may be in the umbilical region if the liver is enlarged or displaced.

Vomiting and Diarrhea.—These symptoms are usually present during some stage of most cases. When the vomiting starts it usually persists.

Jaundice.—Jaundice was present in 69 per cent. of the cases in Musser's series. It may be due to gall-stones or to an inflammatory condition, or to the carcinoma. If due to the extension or to the pressure of the new growth it is usually continuous and progressive. If due to an inflammatory condition or to gall-stones it may be intermittent.

Interference with the general health may be the first indication of malignant disease of the gall-bladder. Rapid loss of flesh and strength follow quickly after the onset of the disease. Anemia is marked, but its appearance in the skin may be obscured by the jaundice. In the last stages the patient may become drowsy and finally comatose.

Ascites.—Ascites occurs, according to Rolleston, in 25 per cent. of the cases. It is not due to the malignant

growth in the gall-bladder, but to the secondary growths, particularly the chronic peritonitis due to metastases in the peritoneum. It may be due to pressure on the portal vein.

Duration.—The disease usually terminates within six months or a year.

Complications.—The gall-bladder may rupture, causing a fatal hemorrhage, a general peritonitis, or a general abdominal carcinosis. The gall-bladder may become infected and cause a general peritonitis. By extension of the disease there may be obstruction in the duodenum or in the colon.

The symptoms of carcinoma of the cystic duct are practically the same as those of carcinoma of the gall-bladder. The symptoms of carcinoma of the hepatic duct are practically the same as those of the liver.

Symptoms of Carcinoma of the Common Bile Duct.—*Jaundice.*—Rolleston states that jaundice is usually the first symptom. As a rule it precedes pain. The jaundice is progressive and becomes very marked. At the onset it may be associated with the gastro-intestinal disturbances that accompany the interference of the passage of the bile into the intestines—that is, with nausea, vomiting, constipation, clay-colored stools, etc.

The jaundice differs from that of catarrhal jaundice in being more persistent. Catarrhal jaundice usually disappears spontaneously or as a result of treatment in a few weeks. That due to a malignant disease steadily progresses.

Pain.—Pain may be dull in character and referred to the right hypochondrium or to the epigastrium, or there may be attacks of biliary colic.

Gall-bladder.—The gall-bladder is usually distended and can be palpated unless obscured by ascites.

Course.—This is usually rapid. The duration of life after the appearance of the jaundice is rarely more than six months. This fact is of value in excluding malignant disease of the biliary ducts in cases of jaundice of longer

duration. If the malignant growth involves the cystic duct alone, there is ordinarily no jaundice.

Treatment of Carcinoma of the Gall-bladder and Ducts.—The disease is necessarily fatal unless it is removed. If the growth is limited to the gall-bladder it can be successfully removed, though the mortality is high and an early recurrence is the usual result. It is probable that most cases of successful removal of the gall-bladder for carcinoma were operated upon for gall-stones and the carcinoma was found accidentally.

In a few cases a malignant growth has been removed from the bile duct. The operation is one of difficulty and with a high surgical risk.

An anastomosis of the gall-bladder to the intestines to overcome an obstruction in the common bile duct may relieve the symptoms for a time.

The pain and the gastro-intestinal disturbances may require medical treatment.

CARCINOMA OF THE AMPULLA OF VATER.

The papilla or ampulla of Vater is formed by the junction of the main pancreatic duct and the common bile duct and opens into the middle portion of the duodenum.

Carcinoma of the ampulla of Vater must be distinguished, according to Rolleston, from (1) carcinoma of the termination of the common bile duct, (2) from carcinoma of the termination of Wirsung's duct, and (3) from carcinoma of the duodenum which involves the ampulla of Vater secondarily. Obviously, excepting in a very early stage of the disease, it would not be possible to locate exactly the anatomical part in which the tumor originated, and doubtless many cases described as carcinoma of the ampulla of Vater would not stand this severe test.

Carcinoma of the ampulla of Vater is practically always the columnar variety—that is, the same as found in the bile ducts.

As the carcinoma increases it early forms an obstruction in the pancreatic duct or to the common bile duct, or to both. The tumor is small, and secondary growths are unusual on account of the early termination of the disease.

Age and Sex.—In both age and sex, carcinoma of the ampulla of Vater corresponds to carcinoma of the bile ducts. It is more common in men than in women. Of 19 cases collected by Rolleston 14 were men, 5 women.

The average age in Rolleston's 19 cases was 55.2 years; the extremes were thirty-four and eighty-one years.

Gall-stones.—In only 2 of Rolleston's cases gall-stones were present, which suggests that they have not the same causative influence here as in the gall-bladder. It is possible that they may have been present and passed into the intestine.

Symptoms.—The symptoms of carcinoma of the ampulla of Vater depend on the interference with the functions of the pancreatic and common bile ducts and in a late stage, if the duration of the disease is sufficient, of the duodenum.

Treatment.—Surgically the growth may be removed either by resecting the duodenum or by excision. Oehler reports a case alive and well three years and nine months after the removal of such a growth.

The medical treatment is entirely symptomatic and similar to that for carcinoma of the common bile duct.

CARCINOMA OF THE LIVER.

Carcinoma of the liver may be primary or secondary. Primary carcinoma is rare. Eggel estimated that primary carcinoma was found once in 2000 autopsies.

Sex.—In Rolleston's series of 42 cases of primary carcinoma of the liver there were 29 males and 13 females. In Eggel's cases the proportion was practically the same as in Rolleston's cases.

Age.—The average age of 42 cases collected by Rolleston was 47.2 years. It is rare before forty years of age, but

may occur at any age. P. W. Phillips collected from the literature 11 cases of primary carcinoma of the liver in children and added one of his own, all of which he believed to be genuine cases. It is probable that some cases reported as carcinoma of the liver in children, are multiple adenomata and not carcinomata.

Etiology.—*Cirrhosis of the Liver.*—This is generally considered to be a predisposing cause of carcinoma of the liver, though some observers regard it as a result. The two conditions are certainly frequently found together. Secondary carcinoma more frequently than primary carcinoma of the liver is not associated with cirrhosis. Rolleston believes that the cirrhosis causes a compensatory hyperplasia of the liver cells, and in some cases this change passes into carcinoma.

Multiple adenomata of the liver is a condition in which there is a hyperplasia of the liver cells, and an increase in the connective tissue, such as is seen in cirrhosis of the liver. By some it is believed that the hyperplasia is the result of the cirrhosis, by others that both conditions result from the same cause. The former belief is more generally accepted.

The point of interest is the relationship of the adenomata to primary carcinoma of the liver. Multiple adenomata of the liver are believed to be an intermediate stage between cirrhosis and carcinoma. That is, that the cirrhosis causes the compensatory hyperplasia of the liver cells and later the adenomatous nodules become malignant.

Trauma.—A number of cases of carcinoma of the liver have been reported which were believed to have resulted from traumatism. The cases of primary carcinoma of the liver are so infrequent it is difficult to trace the direct connection between an injury and the malignant growth. The liver is so well protected by the chest wall that the occurrence cannot be frequent.

Pathology.—Primary carcinoma of the liver originates either in the liver cells or in the lining of the small biliary ducts, or of the larger bile ducts.

Primary carcinoma of the liver occurs in several forms.

I. *Primary Massive Carcinoma.*—There is a single rapidly-growing mass of carcinomatous tissue which pushes the liver tissue before it, and which does not show the same tendency to infiltrate the liver as the diffuse form. That is, it remains more localized. There may be secondary nodules in the liver. The liver is considerably but irregularly enlarged especially on the right side.

II. *Primary Infiltrating or Diffuse Carcinoma.*—This forms a diffuse infiltration of a large part of the liver. There is a large amount of fibrous tissue. The liver may not be enlarged and it may have in general the appearance of a cirrhotic liver.

III. *Nodular or Multiple Primary Carcinoma.*—In this form there are multiple nodules throughout the liver and the appearance of the liver is similar to that seen in secondary carcinoma of the liver. It is possible or probable that one nodule was primary and the others secondary to that nodule, or that the primary growth was in another organ and not detected on account of its small size.

In these cases there was frequently, first, a cirrhosis of the liver, and the carcinoma resulted from it, though some observers believe that the carcinoma was the original lesion and caused the cirrhosis.

The cirrhosis is extensive and involves the entire organ.

Secondary Carcinoma of the Liver.—This condition is more common than primary carcinoma of the liver in the proportion of at least 1 to 20 and possibly 1 to 40. It occurs more frequently in women than in men, probably because women are more often the victims of carcinoma, and especially in organs, such as the breast and uterus, from which secondary growths in the liver are especially frequent.

The secondary growths in the liver are practically always multiple and usually scattered throughout the organ. The liver is usually increased in size and may be very large. The surface is rough and studded with hard, white, carcinomatous nodules.

Symptoms of Primary and Secondary Carcinoma of the Liver.—Whether primary or secondary, the symptoms of carcinoma of the liver depend on the extent of the disease, and the involvement of surrounding organs. In the earliest stage there are no symptoms directly referable to the liver, and the liver condition may even be well-marked before it gives symptoms. In many cases of secondary carcinoma of the liver the symptoms are due entirely to the primary lesion and the liver deposit is discovered only at autopsy.

In primary carcinoma of the liver the early symptoms may be general weakness, loss of weight and strength, and only at a later stage is the location of the disease recognized.

Liver.—The size of the liver is usually increased. In some cases the increase in size is so great that the liver seems to fill a large part of the abdomen. The surface of the liver may be nodular or irregular. It is more often smooth in primary than in secondary carcinoma. The right side is more often enlarged than the left. The liver usually moves with respiration, but may become adherent to the abdominal wall.

The enlargement of the liver is steadily progressive, and usually rapid. The great vascularity and physiological activity of the organ doubtless favors the rapid increase of the malignant growth. This may be further accelerated by hemorrhage into it.

In some cases, especially in the massive variety, the growth may be so soft that it fluctuates and resembles an abscess. The tendency for the growth to increase at the periphery, frequently gives a depressed centre or umbilicated form that is characteristic.

Ascites.—This is present in one-half of the cases at some stage of the disease. It may be caused (1) by peritoneal irritation due to extension of the disease to the peritoneum covering the liver or to a secondary deposit elsewhere in the abdominal cavity, or (2) to obstruction to the capillaries inside the liver, or (3) pressure on the

portal vein by extension of the primary or by a secondary growth.

The ascitic fluid is usually clear in color, but if jaundice is also present it is yellow, and if intraperitoneal hemorrhages have occurred it may be bloody.

Jaundice.—This is a frequent symptom, being present in about 50 per cent. of the cases. It is usually due to mechanical obstruction from pressure either on the common bile duct or less frequently to pressure on the larger intrahepatic ducts. Jaundice produced in this way usually begins gradually but is steadily progressive and becomes marked if the disease is sufficiently prolonged. In some cases the onset of jaundice is sudden. The abrupt onsets may be caused by a hemorrhage into the growth causing a sudden increase in its size. A catarrhal jaundice may develop in the early stage of the disease and subside. This is probably the explanation of some cases of intermittent jaundice seen with carcinoma of the liver.

Pain.—Pain is not a marked symptom in carcinoma of the liver. Local discomfort and a sense of weight from the increased size of the liver are more frequent symptoms. When pain is present it is probably due to a perihepatitis and to the peritoneal irritation from the rough surface of the movable liver.

Cachexia.—The onset of cachexia is rapid and progressive. There is marked emaciation, which is particularly noticeable in the face and extremities, in contrast with the abdomen, which may be distended by the enlarged liver and the ascites.

Duration.—White states that the duration of primary carcinoma of the liver is usually less than four months. The duration of the secondary carcinoma of the liver depends on the nature of the primary lesion, which may terminate the life of the patient shortly after the involvement of the liver occurs or is noticed. In other cases life may be prolonged longer than is usual for a primary carcinoma.

Treatment.—The treatment is entirely symptomatic. A few cases have been operated upon and the growth in the liver removed. This, however, is not often done, and it is doubtful if any real benefit can be secured with the present knowledge of operative technique.

CARCINOMA OF THE PANCREAS.

Frequency.—Carcinoma of the pancreas is a frequent form of malignant disease. In Bashford's statistics, in a total of 84,448 deaths from malignant disease in 1901, 1902, and 1903, there were 526 males and 474 females, or about 12 per cent., who died of primary malignant disease of the pancreas. These cases include both carcinomata and sarcomata. It is not easy in the terminal stage in all cases to determine the exact location of the primary lesion and it is possible that in the cases reported, some were secondary growths.

Age.—In Bashford's statistics there were 6 cases under twenty-five years of age, and the largest number of cases were in the decade between fifty-five and sixty-five years. Cases in earlier years are reported in the literature. Wolff refers to a case of primary carcinoma of the pancreas reported by Kühn and another by Sotow in children under two years of age.

Sex.—Carcinoma of the pancreas is more common in men than in women. In Bashford's statistics in 1000 cases of primary malignant disease of the pancreas 526 were men and 474 were women. Of the cancer deaths in men, one in 64 and in women, one in 107 were from primary malignant disease of the pancreas.

Description.—The variety of primary carcinoma is most frequently scirrhus, others, such as medullary, colloid carcinoma, and epithelioma, have been described.

Usually the growth starts in the head of the pancreas, but frequently at the time of the examination it has involved the entire gland.

The most frequent metastases from carcinoma of the

pancreas are in the liver. A number of writers have noted that the deposits in the liver, secondary to carcinoma of the pancreas, are usually of small size. By direct extension the growth most frequently involves the stomach, duodenum, and common bile duct, and the symptoms frequently depend on the secondary involvements. The secondary involvements of the pancreas from these same organs, the stomach, duodenum, and bile ducts, are frequent. Undoubtedly many cases reported to be primary in the pancreas were really secondary to the growths in other organs. When the growth is in an advanced stage, such as is seen frequently at autopsy, it is not possible to state in which organ the growth started.

Symptoms.—*Pain.*—This is one of the earliest and most constant symptoms of carcinoma of the pancreas. It is usually referred to the epigastrium, but may radiate to the back. It may be caused by pressure of the growth on the celiac ganglion and its branches or on the pancreatic or common bile duct. If the pain is due to pressure on the celiac ganglion and its branches, it is usually severe and increases in intensity. If the pain is due to pressure on the pancreatic or common bile duct it may be intermittent and colicky in character.

Tumor.—A tumor can be palpated in about 25 per cent. of the cases, and is usually in the epigastrium. It may be either to the right or the left of the middle line. It is deep-seated and may be obscured by a thick, abdominal wall. It may pulsate with the aorta.

Jaundice.—As carcinoma of the pancreas is most frequently situated in the head, obstruction to the common bile duct with the resulting jaundice is of frequent occurrence. Carcinoma of the pancreas is one of the most frequent causes next to gall-stones, of obstruction to the common bile duct. It may be one of the earliest symptoms. Usually the jaundice is steadily progressive and becomes very marked before death. There may be no jaundice in cases starting in the body or tail of the pancreas.

Gall-bladder.—The condition in the gall-bladder depends on the obstruction to the common bile duct. As a rule the gall-bladder is usually dilated when the obstruction is due to a malignant process and contracted when due to a gall-stone. The gall-bladder follows this rule and is usually dilated in cases of carcinoma of the pancreas.

Liver.—The liver is not usually enlarged. The secondary deposits in the liver, it is stated, are not as large as secondary growths from malignant growths in other organs. Miraillie found the liver enlarged only seventeen times in a series of 113 cases.

Gastro-intestinal Tract.—The disturbance of the gastro-intestinal tract may precede all other symptoms. There may be nausea and vomiting, loss of appetite, distaste for food, etc. If the growth extends to the pylorus it may be obstructed, causing dilatation of the stomach.

By obstruction of the pancreatic duct, or by destruction of the pancreatic tissue, there may be a lack of pancreatic juice in the intestines. It is believed that this causes fatty stools, that are sometimes seen in cases of pancreatic carcinoma.

Diabetes mellitus may appear in a late state of pancreatic carcinoma when the pancreas is largely destroyed by the growth.

Cachexia.—This is usually rapid in its progress. The mechanical obstruction of the growth to the pancreatic and common bile ducts, stomach and intestines and the growth of the tumor and metastases in vital organs all add to the cachexia. The rapid course of the cachexia is of diagnostic value.

Duration.—This is short, usually lasting only a few months. Opie, however, states that the duration of the disease may be two or more years. These cases are exceptional.

Prognosis.—This is always unfavorable.

Treatment.—The medical treatment is largely the relief of symptoms. The administration of trypsin, or a pancreatic extract, may assist in digestion when there is

an absence of pancreatic juice in the intestines. Morphin will probably be necessary for the pain early in the disease.

The surgical treatment is usually directed to relieving the complications. The obstruction to the common bile duct and distention of the gall-bladder may be benefited by a cholecystenterostomy. The results of the surgical removal of the growth itself are not favorable, though it has been done in a number of cases. The primary mortality is very high and life is not greatly prolonged.

LITERATURE.

Dietz. Virchows Arch., Bd. 164, S. 381.
Eggel. Beitr. z. path. Anad., 1901, xxx, S. 506.
Freidheim. Beitz. klin. Chir., Bd. 44, S. 188.
Fütterer. Ueber die Aetiologie des Carcinoma.
Mayo. Collected Papers, 1910.
Miodowski. Virchows Arch., Bd. 169, S. 117.
Musser. Boston Med. and Surg. Jour., vol. cxxi, pp. 525, 553, 581.
Phillips. Zeit. f. Krebsf., Bd. v, S. 357.
Rolleston. Diseases of the Liver and Bile Tract.
Siegert. Virchows Arch., Bd. 132, S. 253.

CHAPTER XII.

CANCER OF THE KIDNEY, BLADDER, PROSTATE, PENIS, AND TESTIS.

CANCER OF THE KIDNEY.

THERE is great obscurity in the pathology and classification of malignant tumors of the kidney. This trouble is caused largely by the difficulty in properly classifying the hypernephromata. Tumors, having practically the same histological characteristics, are called by different observers alveolar sarcoma, perithelioma, endothelioma, angiosarcoma, etc., all of which would better be classified under hypernephromata.

In the three varieties, hypernephromata, carcinomata, and sarcomata, are included most of the malignant growths of the kidney and of these sarcomata are very rare.

Hypernephromata.—The origin of the hypernephromata is still in dispute.

Grawitz, in 1883, was the first to give an accurate description of the hypernephromata. He believed them to originate in the adrenal "rests," and since the appearance of his article, this origin has been widely accepted. Those who accept the adrenal "rests" as the origin of hypernephromata believe that they definitely illustrate Cohnheim's theory of the development of the tumors from fetal inclusions because these adrenal "rests" are frequently seen in an early stage before the development of the hypernephromata.

The evidence offered to prove that hypernephromata develop from adrenal "rests" is that they are more fre-

quently located in the upper pole of the kidney, where adrenal "rests" are most frequent, that the encapsulation of the tumor is similar to that of adrenal "rests;" that the character and arrangement of the cells is similar to that of the normal adrenal gland and unlike that of the kidney, and the fatty infiltration of the cells.

The theory that hypernephromata develop from adrenal "rests" has been rejected by some observers.

Sudeck believed that the tumors described by Grawitz, and now generally termed hypernephromata, were not derived from adrenal "rests," but were derived from renal tubules. Stoerk more recently has expressed his opinion against hypernephromata originating in adrenal "rests," but believes that they are carcinomata developing after an atrophic nephritis. Wilson has also expressed his belief that hypernephromata do not originate in adrenal "rests." He makes the following conclusions:

"1. Most if not all so-called 'adrenal rests' are probably of Wolffian origin.

"2. There is almost no evidence, embryological or histological, in support of Grawitz's hypothesis that the so-called 'hypernephromata' have their origin in adrenal rests.

"3. There is much evidence that the so-called 'hypernephromata' do not arise (according to Stoerk's hypothesis) from proliferations of the adult secreting epithelium of the convoluted tubules.

"4. There is much evidence that the so-called 'hypernephromata' do arise from islands of nephrogenic tissue (primitive renal blastema). Such tissue is sometimes present in the adult kidney, and appears capable of forming tumors of the non-infiltrating, mixed-cordon, tubular, papilloform, and sarcoma type so characteristic of the so-called hypernephromata."

The hypernephromata are usually surrounded by a definite capsule, which may be broken through in places. The formation of the growth varies in different parts of the tumor, in places it has a papillary form and in other

places, tubular. The arrangement and character of the cells in different parts of the growth suggest carcinoma, sarcoma, and adenoma.

The location of the growth may be in any part of the kidney parenchyma. Those who accept Grawitz's theory, and believe that hypernephromata develop from adrenal "rests," claim that these tumors are more common in the upper pole of the kidney. Wilson in a series of 48 cases found 12 to have originated in the upper pole, 14 in the middle, and 10 in the lower, and in 12 cases the exact location was indeterminable.

The *degree of malignancy* of hypernephromata is in the same obscurity as their origin and histology. If it is accepted that they originate in the adrenal rests or fetal inclusions, then it is believed that they have existed for a long time as benign conditions, and later, as a result of injury or other excitant, took on the malignant quality.

The hypernephromata are sometimes divided into benign and malignant, showing the uncertain knowledge of the growth. It is better that all hypernephromata should be considered as malignant growths and treated as such. If it is a benign growth it should not be classified with the usual group known as hypernephromata.

The growth spreads by direct extension and by metastases. The metastases usually occur through the blood-vessels and more rarely through the lymphatic system. In Garceau's series the metastases occurred most frequently in the lungs and bones.

Age.—The ages of 176 cases in a series reported by Garceau arranged by decades are shown in the following table:

1 to 10 years	4 cases.
10 to 20 "	0 "
20 to 30 "	10 "
30 to 40 "	17 "
40 to 50 "	48 "
50 to 60 "	61 "
60 to 70 "	24 "
70 to 80 "	3 "
Not stated	9 "
	176 "

The youngest was eighteen months and the oldest seventy-nine years of age.

Sex.—Of the 176 cases in Garceau's series, 102 were males and 71 females, and in 3 it was not stated. Most writers state that hypernephromata are more frequent in males than in females, and in about the same proportion as in Garceau's series.

Symptoms.—The three cardinal symptoms of a malignant tumor of the kidney are hematuria, pain, and tumor. They are not all necessarily present in all cases.

Hematuria.—This is probably the most frequent and important of the three symptoms.

The frequency of hematuria as a symptom of hypernephromata is seen in the statistics of many observers. In the 176 cases reported by Garceau, hematuria was a prominent symptom during some part of the disease in 89, or one-half of the cases. In 61 cases, or 34.6 per cent., there had been no bleeding up to the time the history was taken. Young quotes the statistics of a number of observers which showed hematuria to be present in 50 to 70 per cent. of the cases of hypernephromata.

Garceau believes that the *cause* of hematuria in the early stages is the congestion of the kidney and in the later stages that it is the extension to the pelvis of the kidney, and the rupture of vessels in the growth.

The *character* of the bleeding is subject to wide variations. The amount may be slight and enough merely to discolor the urine, or it may be enough to make the urine appear to be pure blood. In some cases there are sudden changes from clear urine to a marked hematuria, suggesting that a blood clot had temporarily obstructed the ureter. The collection of blood clots in the bladder may give rise to bladder irritability, tenesmus, frequent urination, etc.

There may be a history of a single attack of hematuria and no further bleeding. For example, McCosh reported a case in which there was an attack of hematuria and no further bleeding until shortly before operation. Usually

the attacks of bleeding in the early stages are at intervals of a few weeks or possibly months, and as the disease advances, the intervals become shorter until finally the bleeding is more persistent.

The *duration* of the bleeding may extend over a number of years. Herb reported a case of hypernephroma at the Mayo Clinic in which hematuria had been present for ten years. Garceau speaks of a similar case of Israel, in which the bleeding had extended over the same period. In most cases it is probable that the bleeding does not last over one year.

The bleeding does not seem to be caused by exercise or bodily movements, as is frequently the case with renal calculi, but usually comes on spontaneously, possibly at night. Direct injury seems to have been the cause of the first attack of bleeding in some cases.

Pain.—In the early stages pain is frequently absent, especially in children. Morris states that it was the first symptom in 35 per cent. of the cases. In Garceau's series pain was definitely stated to be the first symptom in 20 per cent. of the cases.

The pain is usually referred to the lumbar region, and from there it may radiate to the thorax, or down to the pelvis, or to the lower extremity.

It may be a dull, continuous pain; it may be intermittent or it may be colicky.

There are various *causes* for the pain. At first it is probably due to the congestion of the kidney. In the late stages the pain may be caused by the pressure of the primary growth, or its metastases, on the neighboring nerves. A clot of blood obstructing the ureter may cause a distinct renal colic. Hemorrhage into the tumor may cause pain by distending the growth and the kidney.

The pain does not seem to be influenced by exercise or position.

Tumor.—At an early stage no tumor is felt, but ultimately the growth reaches a size that makes it easily palpable. In Garceau's series of 176 cases it was definitely

stated to be present in 143, absent in 17, and not mentioned in 16 cases.

The growth at first retains the general shape of the kidney, and it may reach considerable size before the original contour is lost.

The tumor is at first in the lumbar region, but as it increases in size it grows toward the anterior abdominal wall, as that is the direction of least resistance.

If the tumor starts in the upper pole of the kidney it is at first situated high and concealed by the ribs, later it fills the entire space between the ribs and the iliac bone.

The size of the tumor is frequently large; in fact, hypernephromata are frequently among the largest abdominal tumors.

Normally the colon is situated in front of the kidney, and this is usually the relation that it retains to a tumor of the kidney. The colon is usually pushed somewhat inward as well as forward if the growth reaches a large size.

The tumor is smooth and regular in the early stage of the disease, but after it has broken through its capsule it is more irregular and nodular. Its consistency may be hard or soft or cystic.

Urine.—Blood is present in more than 50 per cent. of the cases, in varying amounts, as has been described. Pus is present in those cases in which there is a pyelonephritis. This condition is unusual.

The *amount* of the urine is usually unchanged. There may be a temporary or a permanent obstruction to the passage of urine from the affected kidney. If it is temporary it is usually due to an obstruction caused either by a blood clot, or more rarely by a piece of the tumor itself. Permanent obstruction is due to involvement of the ureter by the extension of the growth, and is an unusual complication. Garceau records a case of this kind in which there was total anuria on the affected side.

Cystoscopic examination may give information of value. If blood is seen coming from the ureter it demonstrates that the hematuria is caused by a kidney and not a bladder lesion, and also shows which kidney is diseased.

Varicocele.—Guyon, in 1881, and Morris, independently in 1884, called attention to the presence of varicocele in renal tumors. It may be due to pressure or thrombi in the spermatic or other veins as a result of the growth. It is of special suggestive value when it is on the right side, which is the unusual side for a varicocele to be present.

Cachexia.—This is influenced considerably by the metastases. There may be jaundice if the liver or gall-ducts are involved. If there has been extension to the peritoneum, ascites will be present. The bones are frequently involved by secondary growths, and spontaneous fractures may occur. Anemia may be increased by the hematuria, though usually the bleeding from the kidney does not cause marked anemia previous to the cachectic stage.

Duration.—It is difficult to determine the duration of a hypernephroma, because the onset may give no symptoms, and the growth not be suspected until it has existed for some time.

In 32 cases in Garceau's series in which nephrectomy was performed the average duration from the beginning to the end was three and one-half years. In this series the total duration of two cases was less than one year, of 10 cases between one and two years, and of 2 cases more than ten years.

In another series of 18 cases reported by Garceau in which no kidney operation was performed, and in which there were metastases, mostly in the bones and liver, the average duration of the disease was only one and a quarter years.

Diagnosis.—With *renal calculus* the kidney is ordinarily not as greatly increased in size as in a hypernephroma. The hematuria is less marked and is increased by exercise,

etc. The pain is more characteristically of the colicky type. The history of the passage of a stone from the kidney or bladder is of suggestive value. X-ray pictures may be of definite diagnostic value. It must be remembered that a calculus may exist together with the hypernephroma.

Renal tuberculosis does not usually cause as great enlargement of the kidney as a hypernephroma. The bacteriological examination of the urine, and the inoculation of animals if necessary, should determine the presence or absence of tuberculosis.

Prognosis.—This is unfavorable even after operation. Of the 74 cases in Garceau's series who survived the operation, and whose subsequent source was known, 43 cases had died, 33 from metastases and 10 from various causes, and 31 were still alive. Most of the latter were recent cases. Of the deaths from metastases, 17 were in the first year, 8 in the second, 6 between the second and sixth years, and 1 after the seventh and the tenth years. Hypernephromata follow the usual course of malignant growths in regard to metastases, the largest number in the first year and a few very late.

Scudder reported 12 cases of hypernephroma which were removed, and all excepting one recent case died of metastases.

Treatment.—The operative removal of the affected kidney offers the only hope of a cure. As in other malignant conditions the earlier the operation the more favorable is the ultimate outcome.

The operative mortality is high. The tumor often reaches a large size, and its removal is necessarily an extensive operation. In Garceau's series of 176 cases there were 143 nephrectomies with 33 operative deaths, or a mortality of 23 per cent. In this series are included, some cases in a period of imperfect technique, and the present mortality would be somewhat lower.

CARCINOMA OF THE KIDNEY.

True carcinoma, starting probably in the renal tubules, is one of the forms of malignant tumor of the kidney. The frequency with which it is recorded depends on the classification of the hypernephromata. If none of these tumors is considered carcinoma, then carcinoma of the kidney is rare. Garceau, who groups all hypernephromata separately, found in a series of 42 malignant renal tumors, 33 hypernephromata, 3 carcinomata, 2 sarcomata, and 4 papillary adenomata.

Symptoms.—These are practically the same as those of hypernephromata, and it is rarely possible to differentiate clinically the two tumors. Carcinoma of the kidney runs a rapid course and does not reach the large size sometimes attained by the hypernephromata.

Treatment.—The removal of the kidney offers the only hope of a permanent cure. The prognosis, however, is very bad.

SARCOMA OF THE KIDNEY.

It is not possible to state the frequency with which sarcomata of the kidney occur, because in the literature some writers have included cases of hypernephromata and cases of other tumors of apparently embryonic origin as sarcomata.

Pure sarcomata of the kidney which are not associated either with hypernephromata or other tumors of embryonic origin do occur. They may be of the round- or spindle-celled variety. Garceau reported 2 cases of sarcoma in a series of 42 malignant tumors of the kidney.

Sarcomata of the kidney are most frequent in early life. Young records 2 cases, one eighteen months and the other four years of age.

Symptoms.—These are practically the same as the symptoms of hypernephromata, from which it is usually impossible clinically to diagnose sarcoma of the kidney. Sarcoma of the kidney is usually seen in early life, though

it occurs in adults. The course is usually rapid and quickly fatal.

Treatment.—The early removal of the growth offers the only hope of a cure. The prognosis, as with other malignant tumors of the kidney, is bad.

MALIGNANT ADENOMA OF THE KIDNEY.

Histologically this tumor closely resembles the benign adenoma. Clinically, however, it shows definite characteristics of a malignant growth. It is an infrequent form of kidney tumor.

The symptoms and treatment are similar to those of other malignant tumors of the kidney. It does not form the large growths seen with hypernephromata.

In addition to the tumors of the kidney that have been described, there are growths of embryonic origin that are occasionally seen which have some characteristics of malignant tumors.

In the pelvis of the kidney and ureter, an epithelioma is occasionally seen.

CARCINOMA OF THE URINARY BLADDER.

Incidence.—In Bashford's statistics there was one death from a malignant growth of the bladder or urethra in each 55 cancer deaths. This is approximately the frequency with which malignant vesical tumors are recorded by different writers.

Sex.—In Bashford's statistics the proportion of males to females was as 2.2 to 1. In Judd's series of 114 bladder tumors (three of which were benign) there were 84 males and 30 females.

Age.—The ages of 111 cases of malignant growths of the urinary bladder in Judd's series are shown in the following table:

10 to 20 years	3	cases.
20 to 30 "	5	"
30 to 40 "	11	"
40 to 50 "	16	"
50 to 60 "	34	"
60 to 70 "	29	"
70 to 80 "	12	"
80 to 90 "	1	"
	111	"

The average of these cases was fifty-three years. The age of the youngest with carcinoma, was seventeen years, and the oldest, also with carcinoma, was eighty-three years.

Etiology.—The cause of malignant tumors of the bladder are probably the same as in other organs of the body. Chronic inflammation and chronic irritation are frequently referred to as etiological factors, and those agents which cause these conditions are believed to influence the formation of malignant growths.

Vesical Calculi.—Calculi seemed to have caused cancer in some cases, though the percentage is apparently not large. In Judd's series of 111 malignant growths, vesical calculi were present in only 2 cases. In these 2 cases, however, the history of stone was longer than that of the tumor.

Parasites.—There are frequent references in the literature to the influence of bilharzia, a species of trematodes in the development of cancer of the bladder.

This parasite according to Stiles is found in Africa, Asia, Cuba, Porto Rico, Panama and probably more generally in tropical and subtropical countries.

The parasites or their ova work into the bladder, as well as into other organs, and hematuria is one of the common symptoms. It is probable that the ova act as irritants to the bladder mucous membrane, and the cancer is caused by the chronic irritation or the chronic cystitis. It must not be assumed that all cases of bilharziosis develop vesical growths. Wolff quotes Goebel,

who found 89 vesical tumors in 1684 cases of bilharziosis, about 50 per cent. of which were malignant.

Chemical Irritation.—By absorption the mucous membrane of the bladder of workers in aniline dyes, naphthol, and other coal-tar products is irritated, and cancer of the bladder may result.

Pathology.—The most common varieties of malignant tumors of the bladder are the papilloma, carcinoma, and sarcoma. Sarcomata are rare.

Papilloma.—These are the most frequent of the bladder tumors. There is a central trunk composed of fibrous tissue, bloodvessels, etc., and covered with transitional epithelium. From this central trunk, there are various branches, forming a villous tumor.

In size the papillomata vary from a split pea to an orange. They are most frequently situated at the base of the bladder, often near the ureteral orifices, and rarely on the fundus. The tumors may be either pedunculated or sessile and are frequently (40 per cent.) multiple.

Histologically these tumors are benign, but clinically they have several characteristics of malignant growths, and they should be treated as such. If they are removed, they tend to recur, sometimes at the place of the original growth, often in another part of the bladder. The recurrences may be multiple, suggesting that they are the result of the implantation of tumor cells on the bladder mucous membrane.

There is a great tendency for the papilloma to undergo a carcinomatous change, and doubtless many of the carcinomata began in a papilloma.

Carcinoma.—These growths in the bladder appear in two forms: the papillomatous and the infiltrating. The *papillomatous* form suggest a transformation of a benign villous tumor, but some are doubtless malignant from the start. In carcinoma the villi are more stunted, and there is a greater tendency to involve the bladder wall than in the papilloma.

The *infiltrating* carcinoma takes the form of an ulcera-

tion surrounded by an elevated margin. It may extend and involve a large part of the bladder.

Sarcoma of the bladder is rare. It is most frequent in early life. In Judd's series of 111 cases of malignant tumors of the bladder, there was no case of sarcoma.

Metastases.—The metastases of vesical tumors occur late and are mostly through the bloodvessels, as there are very few lymphatic vessels in the bladder.

Symptoms.—*Hematuria.*—This is the characteristic symptom of all malignant tumors of the bladder. In papillomata it may be the only symptom. The blood is usually well mixed with the urine. The amount of blood varies from a small discoloration of the urine to a large amount. At the end of micturition nearly pure blood may be passed. There may be an attack of hematuria, and no repetition of it for some weeks or months. The hematuria appears without apparent cause, and does not seem to be influenced by exertion or movement as with vesical calculi. The absence of other symptoms than the hematuria, is most characteristic of papilloma of the bladder.

In carcinoma, certainly after the disease is well advanced, the bleeding is more continuous and associated with other symptoms.

In Judd's series, including both carcinomata and papillomata, hematuria was the initial symptom in 47 per cent. of the cases. Howard states that hematuria is the first symptom in 90 per cent. of cases of carcinoma of the bladder.

Frequency of Urination.—Frequent urination was present in 57 cases in Judd's series. This is a common symptom of carcinoma of the bladder and is due in part to the new growth and in part to the accompanying cystitis. It is sometimes present with clear urine and no signs of cystitis.

Retention.—Retention of urine may be caused by an obstruction by a pedunculated papilloma or by the extension of the carcinoma to the urethra. It is an infrequent symptom.

Pain.—Pain may be due to the tumor, to the cystitis, or to the blood clot. It was present in 88 of Judd's cases. It may be constant or only with micturition.

Urinary Analysis.—Pieces of tumor in the urine are sometimes found in cases of papilloma. If they are found, they are diagnostic. The amount of blood may be only microscopic but usually the quantity is large. Pus is more frequently present in the ulcerated carcinoma than in cases of papilloma of the bladder.

Cystoscopic examination will usually establish the diagnosis. If necessary in some cases a piece of the growth can be removed for microscopic examination.

Duration.—In Judd's 111 cases the average duration of symptoms before the patient came for treatment was 36.59 months. Fourteen cases gave a history of over five years. This long duration indicates that the first symptoms were of a benign lesion, as a malignant growth would not average such a long course. Howard states that the average duration of life after the first symptoms of a carcinoma is under three years.

Prognosis.—The immediate and ultimate results of operative treatment of malignant tumors of the bladder depend on the extent of the growth. Unfortunately most cases are operated upon in an advanced stage, when the operative mortality is high and early recurrence is frequent.

Treatment.—Papillomata of the bladder should always be removed. It is probable that most of them would ultimately become malignant if not removed. Furthermore, it is not possible to determine the nature of the growth, and to know that it is not malignant, except by removal.

For small multiple papillomata and for recurrences the high-frequency current is of special value. It is also used for single tumors. The removal of the growth and a portion of the bladder wall, through a suprapubic or a transperitoneal incision, is probably the best operation for a papilloma of the bladder. Care must be taken to

avoid the implantation of the tumor cells on the bladder mucous membrane.

For carcinoma of the bladder the removal of the growth with a part or the whole of the bladder is the most promising treatment.

If the entire bladder is removed the ureters are implanted into the vagina, or are brought out in the lumbar region. The implantation of the ureters into the rectum is associated with too great risk of renal infection.

The palliative treatment is directed to the relief of symptoms. For the hematuria, irrigation of the bladder may be necessary. If it is impossible to wash out the blood clot an evacuator may be used, or a suprapubic or vaginal drain may be indicated.

For the pain it is best to use morphin and bladder irrigations. It may be necessary to drain the bladder, but this should not be done unless unavoidable, as it may increase and not relieve the discomfort.

CARCINOMA OF THE PROSTATE.

Frequency.—In Bashford's mortality statistics there were 293 deaths from cancer of the prostate in a total of 33,788 male cancer deaths, or 0.86 per cent. of the cancer mortality of males.

Young in private practice found 68 cases of carcinoma of the prostate during a period in which he had 250 cases of benign hypertrophy of the prostate; that is, 21 per cent., were malignant. Wilson and McGrath found in a series of 468 reëxamined prostates 16.5 per cent. were malignant. These statistics indicate that cancer of the prostate is more frequent than formerly believed.

Most of the malignant growths of the prostate are carcinomata. Sarcomata occur in the prostate only rarely.

Age.—The ages of the 293 cases in Bashford's statistics taken from the mortality records of England and Wales are given in the following table:

Under 25 years	1	case.
25 to 35 "	2	cases.
35 to 45 "	4	"
45 to 55 "	26	"
55 to 65 "	81	"
65 to 75 "	112	"
75 to 85 "	62	"
85 "	5	"
	293	"

It will be noticed by these statistics that cancer of the prostate occurs at an advanced age, even later than most cancers of other organs.

Malignant tumors of the prostate, however, occur in early childhood. These early cases are usually sarcomata.

Etiology.—Hypertrophy of the prostate is regarded as a possible factor in the development of carcinoma of the prostate. It is, of course, impossible to prove definitely the relationship. By analogy, however, chronic inflammation of the prostate has the same influence on the development of cancer as chronic inflammation elsewhere.

A chronic posterior urethritis resulting from a gonorrheal infection may be influential in causing a cancer of the prostate in the same manner.

Pathology.—Carcinoma of the prostate may be of the simple or scirrhus variety. It begins usually in the posterior lobe. Usually the prostate is increased in size; it may be of normal size, and sometimes it is atrophic. There may be a number of foci throughout the gland giving it a nodular appearance. In consistency the gland is usually hard. The hardness is of diagnostic help.

In some cases the extension of the growth may be slow, and it may remain limited to the gland itself. In other cases it rapidly extends through the capsule of the prostate and involves the bladder, the rectum, and the pelvic glands, so that in a short time the entire pelvis is infiltrated with the malignant growth. As a rule, the extension of a prostatic cancer is first backward, involving first the seminal vesicles and ejaculatory ducts and then the

bladder. The ureters may be obstructed. The rectum is probably involved late or not at all.

Metastases. — The metastases occur most frequently in the bones, especially the vertebræ, femur, and humerus. Of the lymph glands, the iliac, inguinal, and sacral are the first involved. Metastases in the viscera are unusual. The liver and lungs are most frequently involved.

Symptoms.—The early symptoms of carcinoma of the prostate are similar to those of hypertrophy. There may be difficulty in starting the act of micturition, decrease in the force and increase in the frequency of the act. There may be residual urine in the bladder, though this is not a usual symptom. There may be incontinence late in the disease. The disturbance with urination is progressive and without remissions.

Hematuria.—Hematuria is present in probably 5 to 10 per cent. of the cases of prostatic cancer, and generally indicates extension of the growth and ulceration of the bladder. That is, it ordinarily indicates an advanced stage of the disease. The amount of bleeding is not extensive.

Pain.—This may be the first symptom. It is at first slight, but increases in severity. It may be referred to the penis, bladder, thigh, testes, rectum, legs, etc. When established it is usually constant, and is often increased but not relieved by micturition. At this stage it is probably due to pressure on nerves.

In a late stage there may be retention of urine with cystitis, which gives additional and different pain.

Digital Examination.—The *size and shape* of the gland do not assist greatly in the diagnosis as they are both similar to that of a benign hypertrophy. In carcinoma the enlargement is usually backward between the seminal vesicles and this may be detected by rectal examination in some cases. At a later stage, when the growth has penetrated the capsule of the prostate, the normal shape of the gland may be lost.

The *consistency* of the prostate is of the greatest importance in the differential diagnosis. The stony hardness

of carcinoma usually involves the entire gland but may be limited to one part, and generally distinguishes it from hypertrophy.

The *surface* of the prostate in the early stage is usually smooth, later it may be nodular. The irregular and nodular surface suggests that the disease has penetrated the capsule.

Young states that when the prostate has been exposed at operation, carcinoma can usually be diagnosed by palpation and inspection. If necessary a piece of tissue can be removed for frozen section before continuing the operation.

Prognosis.—This is unfavorable even if the case is seen at an operable stage. In most cases there is an early recurrence. There is, however, definite prolongation of life and an increase of comfort, obtained by operation in many cases.

Treatment.—The radical operation consists in the removal of the prostate gland together with the seminal vesicles, ejaculatory ducts, and the base of the bladder. This operation is an extensive one and the results are still uncertain.

The treatment of the inoperable cases is directed to the symptoms. For pain, morphin and belladonna will be necessary. If there is frequent and painful urination, catheterization and irrigation of the bladder may be necessary. Only soft catheters should be used. In some cases a suprapubic drainage of the bladder is necessary.

CARCINOMA OF THE PENIS.

Frequency.—The frequency of carcinoma of the penis is given by different writers between 1 and 3 per cent. of all carcinomata in males. In Bashford's statistics, malignant disease of the penis is recorded with that of the testes, and as malignant disease of these two organs occurred only 469 times in a total of 33,788 cancer deaths, or approximately in the ratio of 1 in 72, and as the testes are more

frequently involved than the penis, the percentage of carcinoma of the penis is small.

Bashford's cases must have been considerably less than 1 per cent. of the total male cancer deaths. The penis is therefore an infrequent location for a malignant disease.

Age.—Creite tabulated the ages of 616 cases from the literature of eight writers, of which cases there were probably some duplicates, and found the largest number of cases of carcinoma of the penis, 30.5 per cent., in the decade between fifty and sixty years. He himself reported one case of carcinoma of the penis starting in the corpora cavernosa in a child two years of age.

Metastases.—The inguinal glands are generally the first to be involved, but usually they are not diseased until the growth has existed for some months. Küttner states that in some cases the pelvic lymph nodes without the inguinal glands are involved.

Etiology.—*Phimosis.*—This is usually given as an important predisposing cause of carcinoma of the penis. The lack of local cleanliness and the accumulation of secretion beneath the prepuce is believed to cause the irritation that results in the development of the carcinoma. Strong evidence of the influence of phimosis in carcinoma of the penis comes from India, where the disease seems to be more prevalent than in Europe and America. It is stated that in India, carcinoma is common among the Hindoos who do not practice circumcision, but is very rare among the Mohammedans who are circumcised.

Scars.—Scars resulting from injuries, venereal sores, syphilis, etc., are also believed to be etiological factors, acting as scars elsewhere.

Leukoplakia of the glans penis has apparently been the precancerous lesion in some reported cases.

Duration.—The course of carcinoma of the penis is usually slow. The prognosis of the operative removal is much more favorable than in most operations for malignant disease.

Pathology.—Most cases of carcinoma of the penis are epitheliomata. Glandular carcinomata are described though rarely.

The location of a beginning carcinoma of the penis is most frequently in one of three places: (1) the glans penis, especially in the sulcus, (2) on the prepuce, (3) in the corpora cavernosa.

The form may be that of a cauliflower or papillary growth, or of an ulceration.

In the beginning there is most frequently a small wart or thickening of the epithelium, which becomes indurated and extends to the deeper parts, and later takes one of the forms stated. At an advanced stage the penis may be largely destroyed and the ulceration may extend to the abdominal wall and scrotum.

Treatment.—The radical removal of the growth is the only proper treatment. This usually means the amputation of the penis and the removal of the inguinal glands. Excision of the growth without amputation of the penis is sometimes advised, but the results following this less extensive removal cannot be as favorable as the amputation of the penis, and should not be done unless the growth is seen early and favorably located on the prepuce. Subsequent to the operation the case should be carefully watched for any local recurrence, as a subsequent more radical operation might save the patient.

CANCER OF THE TESTIS.

The testis is an infrequent location for either a primary or a secondary malignant growth. In Bashford's statistics the malignant tumors of the penis and testis together constituted 1.4 per cent. of the male cancer deaths. Howard states that only 0.06 per cent. of all male patients admitted to the London Hospital were suffering from a malignant growth of the testis.

Age.—Carcinoma of the testis is a disease of adult life, occurring most frequently in the decade between thirty-

five and forty-five years. Sarcoma of the testis occurs in earlier years; a number of cases are reported in early childhood.

Trauma.—Injury seems to be the exciting factor in an important percentage of the cases of malignant tumors of the testis. Löwenstein records a number of cases of carcinoma and of sarcoma of the testis which apparently resulted from injury. The time which elapsed between the injury and the development of the malignant tumor varied from five weeks to a number of years. It is probable in some cases that the injury directed attention to a preëxisting tumor and was not the direct cause of it. An undescended testis, that is, one that is retained in the abdomen, is more frequently affected by a malignant growth than one that is normally situated.

Pathology.—The classification of malignant tumors of the testis is difficult, as it is complicated by the teratomata, the pathology of which, in the testis as elsewhere, is not clear. In addition to the teratomata, sarcomata and carcinomata are the most frequent malignant tumors of this organ.

Sarcoma.—Formerly this was considered to be more frequent in the testis than carcinoma, but at present it is believed to be less frequent. Formerly under the name of alveolar sarcoma, were grouped tumors that are now classed as carcinoma. Round-celled sarcoma is the most frequent variety in the testis. Spindled-celled occurs but very rarely. The tumor usually grows rapidly and often involves both testes. Probably many of the cases classified as sarcoma really belong to the class of teratomata.

Carcinoma.—The medullary carcinoma is the most common and the scirrhus the less frequent variety. The testis is increased in size, and in the early stages freely movable from the skin. Later the skin becomes adherent, and ulceration of the growth occurs. As with sarcomata, probably many cases diagnosed as carcinoma are really teratomata.

Teratoma (Mixed Tumor). — The origin of these tumors is still the subject of wide differences of opinion. Each theory seems to have some objection and fails to adequately explain some important points. Formerly it was believed that these growths resulted from *fetal inclusions.* That is, a second fetus had partly developed and formed the nucleus from which the tumor developed.

Later the theory of parthenogenesis was used to explain the origin of these growths. It was believed that certain undeveloped cells, partially fertilized in the testis, produced the teratoma.

Ewing, after an extensive analysis of the various hypotheses as to the origin of teratoma, concludes "that teratoma testis arises from sex cells in the neighborhood of the rete, whose normal development into spermatogoma has been suppressed but whose potencies remain intact and ready to express themselves in the various forms of simple and complex teratomata." The teratomata are derived from two or all three original cell layers, and may contain various tissues such as hair, muscle, teeth, cartilage, epidermis, etc. In these tissues, there may be developed growths resembling either carcinoma or sarcoma. Many cases called sarcoma or carcinoma are undoubtedly teratomata.

Symptoms.—*Pain.*—In the early stage there is no pain from the tumor itself except that which is caused by the increased size and weight of the growth. This causes a dragging pain in the back or groin. Later there may be abdominal pain from metastases.

Testicular sensation is usually absent in the later stages when the growth has well developed, and most of the testis has been destroyed.

At first the growth is smooth and freely movable, but later becomes irregular and adherent to the skin, and still later ulcerated.

There may be an effusion into the tunica vaginalis though this is not common. The testis itself is usually hard, though it may be cystic.

Prognosis.—Some of the tumors of the testis are very malignant and form metastases early. In some cases the primary tumor in the testis is found only at autopsy. It is not possible to give definite statement in regard to the percentage of cures following operation for malignant growth of the testis. If the case is operated on early, it should be associated with a low operative mortality and a high percentage of cures.

Treatment.—The only curative treatment is the removal of the testis. The removal of the testis is indicated, not only as a curative, but also as a palliative measure. The removal of the testis is associated with a small risk and it prevents the ulceration that will ultimately occur in most cases. It is better therefore to remove the external growth if possible, as it adds to the comfort of the patient.

LITERATURE.

Creite. Deut. Zeit. f. Chir., Band lxxix, S. 305.
Ewing. Surgery, Gynecology and Obstetries, xii, 258.
Garceau. Tumors of the Kidney.
Goebel. Zeit. f. Krebs., Band iii, S. 369.
Grawitz. Virehows Arehiv, Bd. xeiii, S. 39.
Herb. Amer. Jour. Med. Sei., cxxix, 1011.
Howard. Choyce's Surgery, ii, 870.
" Choyce's Surgery, ii, 942.
Judd. Colleeted Papers, Mayo Clinic, 1912.
Küttner. Beitr. f. klin. Chir., Band xxvi, S. 1.
Löwenstein. Ueber Unfall und Krebskrankheit.
MeCosh. Annals of Surgery, xxxix, 300.
Morris. Surgieal Diseases of the Kidney and Ureters.
Scudder. Annals of Surgery, xliv, 855.
Stiles. Osler's Modern Medieine, i, 550.
Stoerk. Beiträge z. Anat. u. allcg. Path., 1908, Bd. xlii, S. 393.
Sudeck. Virchows Arehiv, Band exxxvi, S. 293.
Sutherland. Indian Medieal Gazette, May, 1902, p. 164.
" Indian Medical Gazette, May, 1905, p. 163.
Wilson. Collected Papers, Mayo Clinic, 1910.
Wilson and McGrath. Colleeted Papers, Mayo Clinic, 1911.
Young. Osler's Modern Medicine, vi, 347.
" Osler's Modern Medicine, vi, 300.

INDEX.

A

Acetone in carcinoma of cervix, 159
Adenocarcinoma of stomach, 219
Adenomata of liver, 293
  malignant, of kidney, 310
  as precancerous lesions, 63
Adhesions, extension of cancer by, 80
Adrenal "rests," 301
Age in development of cancer, 38
  extremes of, 40
Alcohol in mouth cancer, 175
Anastomosis, intestinal, 258
Animals, susceptibility of, to cancer, 38
Appendix, carcinoma of, 268
    etiology of, 268
    pathology of, 270
    symptoms of, 272
Arteries, metastases by, 77
Ascites in carcinoma of gall-bladder, 289
  of liver, 295

B

Benign growths as precancerous lesions, 59
  tumor, definition of, 19
    occurring with malignant, 101
Bile duct, common, carcinoma of, 290
  ducts, carcinoma of, 284, 286
Bladder, involvement of, in carcinoma of cervix, 139
  urinary, carcinoma of, 310
Bladder, urinary, carcinoma of, duration of, 314
    etiology of, 310
    metastases of, 313
    pathology of, 312
    prognosis of, 314
    symptoms of, 312
    treatment of, 314
    urine in, 314
Blood in carcinoma, changes and causes of, 86
  of stomach, 230
Bone, traumatic cancer in, 35
Bougies in diagnosing carcinoma of esophagus, 209
Bowels in carcinoma of stomach, 229
Breast, cancer of, lactation and, 106
  carcinoma of, 103
    age and, 104
    in both breasts, 110
    civil state and, 104
    etiology of, 104
    extension of, 111
      to bones, 113
      lymphatic, 111
      visceral, 113
    frequency of, 103
    location of, 109
    medullary, 109
    mortality statistics of, 104, 123
    pathology of, 108
    permanent cure of, 124
    permeation of, 115
    recurrences of, 124
    relation of affected sides to, 109
    Roentgen rays in, 121

Breast, carcinoma of, scirrhus, 108
sex and, 104
statistics of cures of, 124
symptoms of, 117
treatment of, 120
radium in, 121
mastitis of, 105
chronic cystic, 106
multiple tumors in, 101
sarcoma of, 103, 125
trauma in relation to cancer of, 36, 108
Buccal cavity, carcinoma of, 169
etiology of, 170
Burns in carcinoma of lip, 189

C

Cachexia, 84, 88
in carcinoma of stomach, 229
in malignancy of kidney, 307
Calculus in carcinoma of bladder, 311
Cancer à deux, 64
age and, 38
anthracine, 28
antitoxic substances in, 92
blood changes in, 86
care in manipulation of, 68
cause of, 26
cells, fate of, in circulation, 82
in lymphatic glands, 83
quiescence of, for long periods, 98
scattering of, 69
characteristics of, 18
in city and country, 48
coma in, 89
contagiousness of, 64
cure of, after incomplete operation, 95
definition of, 17
emaciation in, 88
extension of, by adhesions, 80
by contact, 79
by implantation, 79
in mucous membrane, 80
in serous membrane, 79
on skin, 82
families, 42
Cancer, fever in, 89
frequency of, 19
geographical distribution of, 44
heredity in, 41
increase of, 19, 20
infection by wounds, 66
influence of civilization on, 22
juice, 64, 85
in mice, 65
organisms in, 26
pain in, 88
permeation of, 114
post-traumatic, 36
precancerous lesions in, 50
predisposition to, 37
rate of growth in, 18
recurrences of, 67
relation to race to, 44
relative deaths in, 20
removal of piece for diagnosis of, 69
sex and, 40
spontaneous cure of, 90
after erysipelas, 97
of primary growth, 96
statistics of, general, 19
mortality, 39, 46
theories of, 23
toxins of, 85
varieties of, 17
Carcinoma, age incidence of, 40
of ampulla of Vater, 291
of appendix, 268
of bile ducts, 284, 286
of breast, 103
of cervix uteri, 137
of cheek, 183
of duodenum, 247
of esophagus, 204
of face, 194
in fibroma uteri, 62
of fundus uteri, 142
of gall-bladder, 284
of gums, 186
of ileum, 250
of intestines, 244
of jejunum, 250
of kidney, 309
of large intestine, 251
of lips, 187
of liver, 284

Carcinoma, occurrence of, with sarcoma, 99
of palate, 185
of pancreas, 297
of penis, 318
of prostate, 315
rate of growth of, 18
of rectum, 272
spontaneous cure of, 90
of stomach, 212
colloid, 219
scirrhus, 219
of testis, 320
of tongue, 176
of urinary bladder, 310
of uterus, 128
Cardiac orifice, carcinoma of, 242
Caustics in carcinoma of cervix, 158
Cautery, deep action of, 96
in prevention of recurrence, 71
Cervix uteri, carcinoma of, 152
acetone in inoperable cases of, 159
causes of post-operative deaths in, 161
caustics in inoperable cases of, 158
cauterization of, 158
contact infection in, 81
diagnosis of, 152
extension of, 138
fistulæ development of, 139
fixation of uterus in, 139
inoperable cases of, 140, 157
involvement of bladder in, 139
of fundus uteri in, 141
of rectum in, 139
of ureters in, 139
of vagina in, 141
metastases of, 140
operable cases of, 153
operation for, 156
operative statistics of, 160
pathology of, 137
percentage of operability of, 157
recurrences of, 162
symptoms of, 144
Cheek, carcinoma of, 169, 183
Child-birth in breast cancer, 105
trauma of, 36
"Chimney sweepers' cancer," 27
Cirrhosis in carcinoma of liver, 293
Civilization, influence of, on cancer, 45
Climate, cancer and, 44
Cohnheim theory of cancer, 23
Colostomy in carcinoma of large intestine, 258
of rectum, 282
Coma in cancer, 89
Concretions in carcinoma of appendix, 269
Constipation in carcinoma of large intestine, 254
of rectum, 275, 277
in gastric carcinoma, 229
Contact, extension of cancer by, 79
Cystoscopy, in hypernephromata, 307

D

Duodenum, carcinoma of, 247
prognosis, 249
symptoms, 247
treatment, 249
Dysphagia in carcinoma of esophagus, 207
Dyspnea in carcinoma of esophagus, 208

E

Eczema followed by cancer, 53
Emaciation, 88
in carcinoma of esophagus, 208
Embryonal cells, 23
Epulis, 201
Erysipelas in spontaneous cure of cancer, 97
Esophagoscope, diagnostic use of, 209
Esophagus, carcinoma of, 204
etiology of, 204
diagnosis of, 208
dysphagia in, 207

Esophagus, carcinoma of, emaciation in, 208
extension of growth in, 206
metastases of, 206
pathology of, 205
symptoms of, 207
treatment of, 210
Eye in sarcoma of upper jaw, 201

F

Face, carcinoma of, 194
etiology of, 194
frequency of parts involved in, 196
pathology of, 195
symptoms of, 197
treatment of, 197
liquid air in, 197
Family, cancer in, 42
Feces in carcinoma of large intestine, 256
in sarcoma of intestines, 267
Females, greater frequency of cancer in, 41
Fever in cancer, 89
Fibromata uteri as precancerous lesions, 61
Fissures in carcinoma of lips, 189
Fistula as precancerous lesion, 55
with carcinoma of cervix uteri, 139
Flatulence in carcinoma of large intestine, 255
Fundus uteri, carcinoma of, 142
diagnosis of, 148, 150, 152
extension of, 143
inoperable cases of, 157
operable cases of, 155
operation for, 156
operative statistics of, 161
pathology of, 142
recurrences of, 162
symptoms of, 148
treatment of, 155

G

Gall-bladder, carcinoma of, 284
ascites in, 289
etiology of, 285
Gall-bladder, carcinoma of, frequency of, 284
jaundice in, 289
pathology of, 287
symptoms of, 288
treatment of, 291
sarcoma of, 287
Gall-stones in carcinoma, 286
Gastro-enterostomy in carcinoma of pylorus, 241
Gastro-intestinal tract, contact cancer in, 82
multiple tumors in, 101
Glossitis, chronic, 51
Gout in oral cancer, 175
Gums, carcinoma of, 169, 186

H

Handley's theory, 114
Hematuria in carcinoma of bladder, 313
of kidney, 304
of prostate, 317
in hypernephromata, 301
Hemoglobin, changes in, 87
Hemorrhage in carcinoma of rectum, 278
of stomach, 230
Hemorrhoids, relation of, to rectal carcinoma, 274
Heredity, 41
in carcinoma of stomach, 215
Highmore, antrum of, in sarcoma of jaw, 200
Hydrochloric acid in carcinoma of stomach, 234
Hypernephromata, 301
diagnosis of, 307
etiology of, 303
hematuria in, 304
malignancy of, 303
prognosis of, 308
symptoms of, 304
treatment of, 308
urine in, 306

I

Ileum, carcinoma of, 250
Implantation, cancer extension by, 79

Inflammation, chronic, relation of, to cancer production, 31
Intestinal perforation in carcinoma of large intestine, 256
Intestine, large, carcinoma of, 251
etiology of, 251
location of growth in, 252
metastases in, 257
mortality of, 263
prognosis of, 257
symptoms of, 254
treatment of, 257
Intestines, carcinoma of, 244
etiology of, 244
pathology of, 246
statistics of, 244
sarcoma of, 246
etiology of, 264
feces in, 267
pathology of, 265
symptoms of, 266
treatment of, 268
Irritation, chemical, 27
chronic, in carcinoma of face, 195
of lips, 189
of tongue, 177
in mouth cancer, 173, 183
physical, 29

J

Jaundice in carcinoma of common bile duct, 290
of gall-bladder, 289
of liver, 296
of pancreas, 298
Jaw, sarcoma of, 169, 197
metastases in, 200
mortality of, 203
pathology of, 198
prognosis of, 202
symptoms of, 200
treatment of, 202
Jejunum, carcinoma of, 250

K

Kidney, cancer of, diagnosis of, with calculus, 307
Kidney, cancer of, hematuria in, 304
carcinoma of, 309
hypernephromata of, 301
malignant adenoma of, 310
sarcoma of, 301, 309

L

Lactation, relation of, to cancer of breast, 106
Lactic acid in carcinoma of stomach, 234
Large intestine, carcinoma of, 251
Leukocytosis in cancer, 87
Leukoma, 51
Leukoplakia buccalis as a precancerous lesion, 51, 174, 183
Lips, carcinoma of, 169, 187
etiology of, 187
location of, 190
lymphatic extension in, 190
mortality of, 193
pathology of, 189
permanent cure in, 193
prognosis of, 191
symptoms of, 191
treatment of, 191
radium in, 197
contact cancer in, 82
Liquid air in cancer of face, 197
Liver, carcinoma of, 284, 292
ascites in, 295
etiology of, 293
jaundice in, 296
pathology of, 293
symptoms of, 295
treatment of, 297
Lupus vulgaris as a precancerous lesion, 53
Lymphatic glands in carcinoma of breast, 119
of cervix uteri, 140, 162
fate of cancer cells in, 83
metastases in, 75
spontaneous cure in, 92

M

Males, increased cancer death in, 41

Malignant tumors, occurring with benign, 101
Massage, danger in, 68
Mastitis, chronic cystic, 106
preceding carcinoma of breast, 105, 106
Metastases, arterial, 78
in carcinoma of large intestine, 257
lymphatic, 75
modes of production of, 74
peritoneal, 78
relative to viscera, 83
retrograde, 78
spontaneous cure of, 91
venous, 77
Moles, heredity of, 42
as precancerous lesions, 59
Mouse, cancer in, 65
Mucous membrane, implantation of cancer on, 80
Multiparæ, uterine carcinoma in, 131

N

Nævi, heredity of, 42
as precancerous lesion, 59
Nervous system, involvement of, in carcinoma of esophagus, 207
Nipple, retraction of, 109
Nose, involvement of, in sarcoma of jaw, 199
Nulliparæ, uterine carcinoma in, 130

O

Obstruction, intestinal, in carcinoma of large intestine, 255, 257
Operation, incomplete, cure following, 95
Ovary, malignant papilloma of, spontaneous cure of, 91

P

Paget's disease, 53
Palate, carcinoma of, 169, 185
Pancreas, carcinoma of, 297
Papilloma, malignant, of bladder, 312
of ovary, 91
Parasites in carcinoma of bladder, 311
Parasitic theory of cancer, 25
Paraffin, influence of, on cancer development, 28
Penis, carcinoma of, 66, 318
Perforation, intestinal, in carcinoma of large intestine, 256
Peristalsis in carcinoma of large intestine, 255
Peritoneum, metastases in, 78
Permeation of cancer, 114
Phimosis, predisposing to carcinoma of penis, 319
Pipe-smoking in carcinoma of tongue, 178
in development of cancer, 29, 51
Poikilocytosis in cancer, 87
Polyp in carcinoma of large intestine, 254
gastro-intestinal, cancer and, 62
rectal, cancer and, 273
uterine, cancer and, 62
Precancerous lesions, 50, 59
Predisposition, 37
Pregnancy, influence of, on carcinoma of uterus, 163
occurring with carcinoma of uterus, 167
Primary tumors, multiple, 99
spontaneous cure of, 96
Prostate, carcinoma of, 315
etiology of, 316
pathology of, 316
symptoms of, 317
treatment of, 318
Prussia, mortality records in, 39
Ptosis in carcinoma of esophagus, 208
Pylorus, carcinoma of, advanced, 241
operable, 239
treatment of, non-surgical, 241
malignant obstruction of, 236

R

Race, influence of, on cancer, 44
Radium in carcinoma of breast, 121
of face, 197
Rectum, carcinoma of, 272
diagnosis of, 278
inoperable cases of, 281
mortality of, 280, 281
operable cases of, 279
pathology of, 275
symptoms of, 277
treatment of, 279
involvement of, by carcinoma of cervix, 139
Recurrence, 67
arbitrary time limit in, 72
by implantation, 69
late, 72
in operation wounds, 70
prevention of, by cautery, 71
time of, 71
Red blood cells, changes in, 87
"Rests," adrenal, 301
embryonal, 23
Retention, urinary, in carcinoma of bladder, 313
Ribbert's theory of cancer, 25
Roentgen rays in carcinoma of breast, 121
of esophagus, 208
of face, 197
in development of cancer, 30
examination in carcinoma of stomach, 234

S

Sarcoma, age incidence and, 40
of breast, 103, 125
following trauma, 34
of gall-bladder, 287
of intestines, 246, 264
of jaws, 169, 197
of kidney, 301, 309
multiple, of skin, 100
occurrence of, with carcinoma, 99
spontaneous cure of, 90, 99
of testis, 321
Savages, cancer among, 45
Scars, cancer occurring in, 36, 56
Serous membranes, cancer implantation on, 79
Sex incidence of cancer, 40
Sinuses as precancerous lesions, 31, 55
Skin, implantation of cancer on, 82
lesions followed by cancer, 31, 53
Smoking in production of oral cancer, 171, 178
Soot, in development of cancer, 27
Stomach, carcinoma of, 212
blood changes in, 230
cardiac orifice of, 242
contents of, analysis of, 233
diagnosis of, 237
etiology of, 212
extension of, 219
lymphatic, 220
frequency of, 213
hemorrhage in, 230
location of growth in, 224
middle of stomach, 243
mortality of, 214, 240
operation for, 239
pathology of, 219
symptoms of, 224
treatment of, 238
Stricture in carcinoma of rectum, 274
Sun's rays in development of cancer, 30
Syphilis in cancer of oral cavity, 173, 177

T

Tar in development of cancer, 28
Teeth, extraction of, sarcoma of jaw and, 198
in mouth cancer, 174, 177
pain in sarcoma of jaw, 201
relation of, to cancer development, 51
Tenesmus in carcinoma of rectum, 278
Teratoma of testis, 322

Testis, carcinoma of, 320
sarcoma of, 321
traumatic cancer in, 35
Tobacco in cancer of buccal cavity, 172
in development of cancer, 29
Tongue, carcinoma of, 169, 176
diagnosis of, 180
etiology of, 176
metastases in, 179
pathology of, 178
statistics of, 182
symptoms of, 180
treatment of, 182
Toxins of cancer, 85
Trades, influence of, on cancer, 27
Trauma in carcinoma of breast, 108
of large intestine, 253
of liver, 293
of stomach, 216
of testis, 321
in production of cancer, 33
in sarcoma of breast, 125
of jaw, 198
Tumors, definition of, 17
differentiation of, 19
malignant occurring with benign, 101

U

Ulcer in carcinoma of large intestine, 254
of lips, 191
of rectum, 274
relation of, to carcinoma of stomach, 217
Ulceration, chronic, relation of, to cancer development, 31, 54, 55
Ureters, involvement of, with carcinoma of cervix, 139
Urine in carcinoma of bladder, 314
with hypernephromata, 306
Uterine fibromata relation of, to carcinoma, 61
Uterus, carcinoma of, 128
age and, 129
Uterus, carcinoma of, abortions and miscarriages and, 133
cervical erosions and, 136
inflammation and, 136
lacerations in, 134
course of, 151
etiology of, 128
infection of husband and, 66
mixed tumors in, 101
mortality of, 128
in multiparæ, 131
multiple tumors in, 100
in nulliparæ, 130
obstetrical operations and, 134
pathology of, 137, 142
pregnancy in, influence of, 129
occurring with carcinoma, 163
in virgins, 130

V

Vagina, contact cancer in, 81
involvement of, in carcinoma of cervix, 141
Veins, metastases by, 77
Virgins, uterine carcinoma in, 130
Varicocele in tumors of kidney, 307
Varicose ulcers, relation of, to cancer, 54
Vater, ampulla of, carcinoma of, 284, 291
Vomiting in carcinoma of stomach, 227

W

Warts, heredity of, 42
as precancerous lesions, 59
Weather in cancer of face, 195
in carcinoma of lips, 189
influence of, in development of cancer, 30
Wounds, cancer infection of, 66
recurrence of cancer in, 70

LIBRARY OF CONGRESS
0 022 194 753 8